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(71) Applicant: AMGEN INC. [US/US]; Amgen Center, 1840 Dehavilland Drive, Thousand Oaks, CA 91320-1789 (US).

(72) Inventor: OSSLUND, Timothy, D.; 475 Vista Montana, Camarillo, CA 93010 (US).

(74) Agents: ODRE, Steven, M. et al.; Amgen Inc., Amgen Center, 1840 Dehavilland Drive, Thousand Oaks, CA 91320-1789 (US).

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(57) Abstract

Provided herein are granulocyte colony stimulating factor ("G-CSF") analogs, compositions containing such analogs, and related compositions. In another aspect, provided herein are nucleic acids encoding the present analogs or related nucleic acids, related host cells and vectors. In yet another aspect, provided herein are computer programs and apparatuses for expressing the three dimensional structure of G-CSF and analogs thereof. In another aspect, provided herein are methods for rationally designing G-CSF analogs and related compositions. In yet another aspect, provided herein are methods for treatment using the present G-CSF analogs.

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G-CSF ANALOG COMPOSITIONS AND METHODS

Field of the Invention

This invention relates to granulocyte colony stimulating factor ("G-CSF") analogs, compositions containing such analogs, and related compositions. In another aspect, the present invention relates to nucleic acids encoding the present analogs or related nucleic acids, related host cells and vectors. In another aspect, the invention relates to computer programs and apparatuses for expressing the three dimensional structure of G-CSF and analogs thereof. In another aspect, the invention relates to methods for rationally designing G-CSF analogs and related compositions. In yet another aspect, the present invention relates to methods for treatment using the present G-CSF analogs.

Background

Hematopoiesis is controlled by two systems: the cells within the bone marrow microenvironment and growth factors. The growth factors, also called colony stimulating factors, stimulate committed progenitor cells to proliferate and to form colonies of differentiating blood cells. One of these factors is granulocyte colony stimulating factor, herein called G-CSF, which preferentially stimulates the growth and development of neutrophils, indicating a potential use in neutropenic states. Welte et al., PNAS-USA 82: 1526-1530 (1985); Souza et al., Science 232: 61-65 (1986) and Gabrilove, J. Seminars in Hematology 26: (2) 1-14 (1989).

In humans, endogenous G-CSF is detectable in blood plasma. Jones et al., Bailliere's Clinical Hematology 2 (1): 83-111 (1989). G-CSF is produced by fibroblasts, macrophages, T cells trophoblasts, endothelial cells and epithelial cells and is the

expression product of a single copy gene comprised of four exons and five introns located on chromosome seventeen. Transcription of this locus produces a mRNA species which is differentially processed, resulting in two forms of G-CSF mRNA, one version coding for a protein of 177 amino acids, the other coding for a protein of 174 amino acids, Nagata et al., EMBO J 5: 575-581 (1986), and the form comprised of 174 amino acids has been found to have the greatest specific in vivo biological activity. G-CSF is species cross-reactive, such that when human G-CSF is administered to another mammal such as a mouse, canine or monkey, sustained neutrophil leukocytosis is elicited. Moore et al., PNAS-USA 84: 7134-7138 (1987).

Human G-CSF can be obtained and purified from a number of sources. Natural human G-CSF (nhG-CSF) can be isolated from the supernatants of cultured human tumor cell lines. The development of recombinant DNA technology, see, for instance, U.S. Patent 4,810,643 (Souza) incorporated herein by reference, has enabled the production of commercial scale quantities of G-CSF in glycosylated form as a product of eukaryotic host cell expression, and of G-CSF in non-glycosylated form as a product of prokaryotic host cell expression.

G-CSF has been found to be useful in the treatment of indications where an increase in neutrophils will provide benefits. For example, for cancer patients, G-CSF is beneficial as a means of selectively stimulating neutrophil production to compensate for hematopoietic deficits resulting from chemotherapy or radiation therapy. Other indications include treatment of various infectious diseases and related conditions, such as sepsis, which is typically caused by a metabolite of bacteria. G-CSF is also useful alone, or in combination with other compounds, such as other cytokines, for growth or expansion of

cells in culture, for example, for bone marrow transplants.

Signal transduction, the way in which G-CSF effects cellular metabolism, is not currently thoroughly understood. G-CSF binds to a cell-surface receptor which apparently initiates the changes within particular progenitor cells, leading to cell differentiation.

Various altered G-CSF's have been reported. Generally, for design of drugs, certain changes are known to have certain structural effects. For example, deleting one cysteine could result in the unfolding of a molecule which is, in its unaltered state, is normally folded via a disulfide bridge. There are other known methods for adding, deleting or substituting amino acids in order to change the function of a protein.

Recombinant human G-CSF mutants have been prepared, but the method of preparation does not include overall structure/function relationship information. For example, the mutation and biochemical modification of Cys 18 has been reported. Kuga et al., Biochem. Biophy. Res. Comm 159: 103-111 (1989); Lu et al., Arch. Biochem. Biophys. 268: 81-92 (1989).

In U.S. Patent No. 4, 810, 643, entitled, "Production of Pluripotent Granulocyte Colony-Stimulating Factor" (as cited above), polypeptide analogs and peptide fragments of G-CSF are disclosed generally. Specific G-CSF analogs disclosed include those with the cysteins at positions 17, 36, 42, 64, and 74 (of the 174 amino acid species or of those having 175 amino acids, the additional amino acid being an N-terminal methionine) substituted with another amino acid, (such as serine), and G-CSF with an alanine in the first (N-terminal) position.

EP 0 335 423 entitled "Modified human G-CSF" reportedly discloses the modification of at least one amino group in a polypeptide having hG-CSF activity.

EP 0 272 703 entitled "Novel Polypeptide" reportedly discloses G-CSF derivatives having an amino acid substituted or deleted at or "in the neighborhood" of the N terminus.

EP 0 459 630, entitled "Polypeptides" reportedly discloses derivatives of naturally occurring G-CSF having at least one of the biological properties of naturally occurring G-CSF and a solution stability of at least 35% at 5 mg/ml in which the derivative has at least Cys^{17} of the native sequence replaced by a Ser^{17} residue and Asp^{27} of the native sequence replaced by a Ser^{27} residue.

EP 0 256 843 entitled "Expression of G-CSF and Muteins Thereof and Their Uses" reportedly discloses a modified DNA sequence encoding G-CSF wherein the N-terminus is modified for enhanced expression of protein in recombinant host cells, without changing the amino acid sequence of the protein.

EP 0 243 153 entitled "Human G-CSF Protein Expression" reportedly discloses G-CSF to be modified by inactivating at least one yeast KEX2 protease processing site for increased yield in recombinant production using yeast.

Shaw, U.S. Patent No. 4,904,584, entitled "Site-Specific Homogeneous Modification of Polypeptides," reportedly discloses lysine altered proteins.

WO/9012874 reportedly discloses cysteine altered variants of proteins.

Australian patent application Document No. AU-A-10948/92, entitled, "Improved Activation of Recombinant Proteins" reportedly discloses the addition of amino acids to either terminus of a G-CSF molecule for the purpose of aiding in the folding of the molecule after prokaryotic expression.

Australian patent application Document No. AU-A-76380/91, entitled, "Muteins of the Granulocyte Colony Stimulating Factor (G-CSF)" reportedly discloses muteins of the granulocyte stimulating factor G-CSF in the sequence Leu-Gly-His-Ser-Leu-Gly-Ile at position 50-56 of G-CSF with 174 amino acids, and position 53 to 59 of the G-CSF with 177 amino acids, or/and at least one of the four histadine residues at positions 43, 79, 156 and 170 of the mature G-CSF with 174 amino acids or at positions 46, 82, 159, or 173 of the mature G-CSF with 177 amino acids.

GB 2 213 821, entitled "Synthetic Human Granulocyte Colony Stimulating Factor Gene" reportedly discloses a synthetic G-CSF-encoding nucleic acid sequence incorporating restriction sites to facilitate the cassette mutagenesis of selected regions, and flanking restriction sites to facilitate the incorporation of the gene into a desired expression system.

G-CSF has reportedly been crystallized to some extent, e.g., EP 344 796, and the overall structure of G-CSF has been surmised, but only on a gross level. Bazan, Immunology Today 11: 350-354 (1990); Parry et al., J. Molecular Recognition 8: 107-110 (1988). To date, there have been no reports of the overall structure of G-CSF, and no systematic studies of the relationship of the overall structure and function of the molecule, studies which are essential to the systematic design of G-CSF analogs. Accordingly, there exists a need for a method of this systematic design of G-CSF analogs, and the resultant compositions.

Summary of the Invention

The three dimensional structure of G-CSF has now been determined to the atomic level. From this three-dimensional structure, one can now forecast with

substantial certainty how changes in the composition of a G-CSF molecule may result in structural changes. These structural characteristics may be correlated with biological activity to design and produce G-CSF analogs.

Although others had speculated regarding the three dimensional structure of G-CSF, Bazan, Immunology Today 11: 350-354 (1990); Parry et al., J. Molecular Recognition 8: 107-110 (1988), these speculations were of no help to those wishing to prepare G-CSF analogs either because the surmised structure was incorrect (Parry et al., supra) and/or because the surmised structure provided no detail correlating the constituent moieties with structure. The present determination of the three-dimensional structure to the atomic level is by far the most complete analysis to date, and provides important information to those wishing to design and prepare G-CSF analogs. For example, from the present three dimensional structural analysis, precise areas of hydrophobicity and hydrophilicity have been determined.

Relative hydrophobicity is important because it directly relates to the stability of the molecule. Generally, biological molecules, found in aqueous environments, are externally hydrophilic and internally hydrophobic; in accordance with the second law of thermodynamics provides, this is the lowest energy state and provides for stability. Although one could have speculated that G-CSF's internal core would be hydrophobic, and the outer areas would be hydrophilic, one would have had no way of knowing specific hydrophobic or hydrophilic areas. With the presently provided knowledge of areas of hydrophobicity/-philicity, one may forecast with substantial certainty which changes to the G-CSF molecule will affect the overall structure of the molecule.

As a general rule, one may use knowledge of the geography of the hydrophobic and hydrophilic regions

to design analogs in which the overall G-CSF structure is not changed, but change does affect biological activity ("biological activity" being used here in its broadest sense to denote function). One may correlate biological activity to structure. If the structure is not changed, and the mutation has no effect on biological activity, then the mutation has no biological function. If, however, the structure is not changed and the mutation does affect biological activity, then the residue (or atom) is essential to at least one biological function. Some of the present working examples were designed to provide no change in overall structure, yet have a change in biological function.

Based on the correlation of structure to biological activity, one aspect of the present invention relates to G-CSF analogs. These analogs are molecules which have more, fewer, different or modified amino acid residues from the G-CSF amino acid sequence. The modifications may be by addition, substitution, or deletion of one or more amino acid residues. The modification may include the addition or substitution of analogs of the amino acids themselves, such as peptidomimetics or amino acids with altered moieties such as altered side groups. The G-CSF used as a basis for comparison may be of human, animal or recombinant nucleic acid-technology origin (although the working examples disclosed herein are based on the recombinant production of the 174 amino acid species of human G-CSF, having an extra N-terminus methionyl residue). The analogs may possess functions different from natural human G-CSF molecule, or may exhibit the same functions, or varying degrees of the same functions. For example, the analogs may be designed to have a higher or lower biological activity, have a longer shelf-life or a decrease in stability, be easier to formulate, or more difficult to combine with other ingredients. The

analogs may have no hematopoietic activity, and may therefore be useful as an antagonist against G-CSF effect (as, for example, in the overproduction of G-CSF). From time to time herein the present analogs are referred to as proteins or peptides for convenience, but contemplated herein are other types of molecules, such as peptidomimetics or chemically modified peptides.

In another aspect, the present invention relates to related compositions containing a G-CSF analog as an active ingredient. The term, "related composition," as used herein, is meant to denote a composition which may be obtained once the identity of the G-CSF analog is ascertained (such as a G-CSF analog labeled with a detectable label, related receptor or pharmaceutical composition). Also considered a related composition are chemically modified versions of the G-CSF analog, such as those having attached at least one polyethylene glycol molecule.

For example, one may prepare a G-CSF analog to which a detectable label is attached, such as a fluorescent, chemiluminescent or radioactive molecule.

Another example is a pharmaceutical composition which may be formulated by known techniques using known materials, see, e.g., Remington's Pharmaceutical Sciences, 18th Ed. (1990, Mack Publishing Co., Easton, Pennsylvania 18042) pages 1435-1712, which are herein incorporated by reference. Generally, the formulation will depend on a variety of factors such as administration, stability, production concerns and other factors. The G-CSF analog may be administered by injection or by pulmonary administration via inhalation. Enteric dosage forms may also be available for the present G-CSF analog compositions, and therefore oral administration may be effective. G-CSF analogs may be inserted into liposomes or other microcarriers for delivery, and may be formulated in gels or other

compositions for sustained release. Although preferred compositions will vary depending on the use to which the composition will be put, generally, for G-CSF analogs having at least one of the biological activities of natural G-CSF, preferred pharmaceutical compositions are those prepared for subcutaneous injection or for pulmonary administration via inhalation, although the particular formulations for each type of administration will depend on the characteristics of the analog.

Another example of related composition is a receptor for the present analog. As used herein, the term "receptor" indicates a moiety which selectively binds to the present analog molecule. For example, antibodies, or fragments thereof, or "recombinant antibodies" (see Huse et al., Science 246:1275 (1989)) may be used as receptors. Selective binding does not mean only specific binding (although binding-specific receptors are encompassed herein), but rather that the binding is not a random event. Receptors may be on the cell surface or intra- or extra-cellular, and may act to effectuate, inhibit or localize the biological activity of the present analogs. Receptor binding may also be a triggering mechanism for a cascade of activity indirectly related to the analog itself. Also contemplated herein are nucleic acids, vectors containing such nucleic acids and host cells containing such nucleic acids which encode such receptors.

Another example of a related composition is a G-CSF analog with a chemical moiety attached. Generally, chemical modification may alter biological activity or antigenicity of a protein, or may alter other characteristics, and these factors will be taken into account by a skilled practitioner. As noted above, one example of such chemical moiety is polyethylene glycol. Modification may include the addition of one or more hydrophilic or hydrophobic polymer molecules, fatty

acid molecules, or polysaccharide molecules. Examples of chemical modifiers include polyethylene glycol, alklpolyethylene glycols, DI-poly(amino acids), polyvinylpyrrolidone, polyvinyl alcohol, pyran copolymer, acetic acid/acylation, proprionic acid, palmitic acid, stearic acid, dextran, carboxymethyl cellulose, pullulan, or agarose. See, Francis, *Focus on Growth Factors* 3: 4-10 (May 1992)(published by Mediscript, Mountview Court, Friern Barnet Lane, London N20 OLD, UK). Also, chemical modification may include an additional protein or portion thereof, use of a cytotoxic agent, or an antibody. The chemical modification may also include lecithin.

In another aspect, the present invention relates to nucleic acids encoding such analogs. The nucleic acids may be DNAs or RNAs or derivatives thereof, and will typically be cloned and expressed on a vector, such as a phage or plasmid containing appropriate regulatory sequences. The nucleic acids may be labeled (such as using a radioactive, chemiluminescent, or fluorescent label) for diagnostic or prognostic purposes, for example. The nucleic acid sequence may be optimized for expression, such as including codons preferred for bacterial expression. The nucleic acid and its complementary strand, and modifications thereof which do not prevent encoooding of the desired analog are here contemplated.

In another aspect, the present invention relates to host cells containing the above nucleic acids encoding the present analogs. Host cells may be eukaryotic or prokaryotic, and expression systems may include extra steps relating to the attachment (or prevention) of sugar groups (glycosylation), proper folding of the molecule, the addition or deletion of leader sequences or other factors incident to recombinant expression.

In another aspect the present invention relates to antisense nucleic acids which act to prevent or modify the type or amount of expression of such nucleic acid sequences. These may be prepared by known methods.

In another aspect of the present invention, the nucleic acids encoding a present analog may be used for gene therapy purposes, for example, by placing a vector containing the analog-encoding sequence into a recipient so the nucleic acid itself is expressed inside the recipient who is in need of the analog composition. The vector may first be placed in a carrier, such as a cell, and then the carrier placed into the recipient. Such expression may be localized or systemic. Other carriers include non-naturally occurring carriers, such as liposomes or other microcarriers or particles, which may act to mediate gene transfer into a recipient.

The present invention also provides for computer programs for the expression (such as visual display) of the G-CSF or analog three dimensional structure, and further, a computer program which expresses the identity of each constituent of a G-CSF molecule and the precise location within the overall structure of that constituent, down to the atomic level. Set forth below is one example of such program. There are many currently available computer programs for the expression of the three dimensional structure of a molecule. Generally, these programs provide for inputting of the coordinates for the three dimensional structure of a molecule (i.e., for example, a numerical assignment for each atom of a G-CSF molecule along an x, y, and z axis), means to express (such as visually display) such coordinates, means to alter such coordinates and means to express an image of a molecule having such altered coordinates. One may program crystallographic information, i.e., the coordinates of

the location of the atoms of a G-CSF molecule in three dimension space, wherein such coordinates have been obtained from crystallographic analysis of said G-CSF molecule, into such programs to generate a computer program for the expression (such as visual display) of the G-CSF three dimensional structure. Also provided, therefore, is a computer program for the expression of G-CSF analog three dimensional structure. Preferred is the computer program Insight II, version 4, available from Biosym, San Diego, California, with the coordinates as set forth in FIGURE 5 input. Preferred expression means is on a Silicon Graphics 320 VGX computer, with Crystal Eyes glasses (also available from Silicon Graphics), which allows one to view the G-CSF molecule or its analog stereoscopically. Alternatively, the present G-CSF crystallographic coordinates and diffraction data are also deposited in the Protein Data Bank, Chemistry Department, Brookhaven National Laboratory, Upton, New York 119723, USA. One may use these data in preparing a different computer program for expression of the three dimensional structure of a G-CSF molecule or analog thereof. Therefore, another aspect of the present invention is a computer program for the expression of the three dimensional structure of a G-CSF molecule. Also provided is said computer program for visual display of the three dimensional structure of a G-CSF molecule; and further, said program having means for altering such visual display. Apparatus useful for expression of such computer program, particularly for the visual display of the computer image of said three dimensional structure of a G-CSF molecule or analog thereof is also therefore here provided, as well as means for preparing said computer program and apparatus.

The computer program is useful for preparation of G-CSF analogs because one may select specific sites on the G-CSF molecule for alteration and readily

ascertain the effect the alteration will have on the overall structure of the G-CSF molecule. Selection of said site for alteration will depend on the desired biological characteristic of the G-CSF analog. If one were to randomly change said G-CSF molecule (r-met-hu-G-CSF) there would be 175^{20} possible substitutions, and even more analogs having multiple changes, additions or deletions. By viewing the three dimensional structure wherein said structure is correlated with the composition of the molecule, the selection for sites of alteration is no longer a random event, but sites for alteration may be determined rationally.

As set forth above, identity of the three dimensional structure of G-CSF, including the placement of each constituent down to the atomic level has now yielded information regarding which moieties are necessary to maintain the overall structure of the G-CSF molecule. One may therefore select whether to maintain the overall structure of the G-CSF molecule when preparing a G-CSF analog of the present invention, or whether (and how) to change the overall structure of the G-CSF molecule when preparing a G-CSF analog of the present invention. Optionally, once one has prepared such analog, one may test such analog for a desired characteristic.

One may, for example, seek to maintain the overall structure possessed by a non-altered natural or recombinant G-CSF molecule. The overall structure is presented in Figures 2, 3, and 4, and is described in more detail below. Maintenance of the overall structure may ensure receptor binding, a necessary characteristic for an analog possessing the hematopoietic capabilities of natural G-CSF (if no receptor binding, signal transduction does not result from the presence of the analog). It is contemplated that one class of G-CSF

analogs will possess the three dimensional core structure of a natural or recombinant (non-altered) G-CSF molecule, yet possess different characteristics, such as an increased ability to selectively stimulate neutrophils. Another class of G-CSF analogs are those with a different overall structure which diminishes the ability of a G-CSF analog molecule to bind to a G-CSF receptor, and possesses a diminished ability to selectively stimulate neutrophils as compared to non-altered natural or recombinant G-CSF.

For example, it is now known which moieties within the internal regions of the G-CSF molecule are hydrophobic, and, correspondingly, which moieties on the external portion of the G-CSF molecule are hydrophilic. Without knowledge of the overall three dimensional structure, preferably to the atomic level as provided herein, one could not forecast which alterations within this hydrophobic internal area would result in a change in the overall structural conformation of the molecule. An overall structural change could result in a functional change, such as lack of receptor binding, for example, and therefore, diminishment of biological activity as found in non-altered G-CSF. Another class of G-CSF analogs is therefore G-CSF analogs which possess the same hydrophobicity as (non-altered) natural or recombinant G-CSF. More particularly, another class of G-CSF analogs possesses the same hydrophobic moieties within the four helical bundle of its internal core as those hydrophobic moieties possessed by (non-altered) natural or recombinant G-CSF yet have a composition different from said non-altered natural or recombinant G-CSF.

Another example relates to external loops which are structures which connect the internal core (helices) of the G-CSF molecule. From the three dimensional structure -- including information regarding

the spatial location of the amino acid residues -- one may forecast that certain changes in certain loops will not result in overall conformational changes. Therefore, another class of G-CSF analogs provided herein is that having an altered external loop but possessing the same overall structure as (non-altered) natural or recombinant G-CSF. More particularly, another class of G-CSF analogs provided herein are those having an altered external loop, said loop being selected from the loop present between helices A and B; between helices B and C; between helices C and D; between helices D and A, as those loops and helices are identified herein. More particularly, said loops, preferably the AB loop and/or the CD loop are altered to increase the half life of the molecule by stabilizing said loops. Such stabilization may be by connecting all or a portion of said loop(s) to a portion of an alpha helical bundle found in the core of a G-CSF (or analog) molecule. Such connection may be via beta sheet, salt bridge, disulfide bonds, hydrophobic interaction or other connecting means available to those skilled in the art, wherein such connecting means serves to stabilize said external loop or loops. For example, one may stabilize the AB or CD loops by connecting the AB loop to one of the helices within the internal region of the molecule.

The N-terminus also may be altered without change in the overall structure of a G-CSF molecule, because the N-terminus does not effect structural stability of the internal helices, and, although the external loops are preferred for modification, the same general statements apply to the N-terminus.

Additionally, such external loops may be the site(s) for chemical modification because in (non-altered) natural or recombinant G-CSF such loops are relatively flexible and tend not to interfere with

receptor binding. Thus, there would be additional room for a chemical moiety to be directly attached (or indirectly attached via another chemical moiety which serves as a chemical connecting means). The chemical moiety may be selected from a variety of moieties available for modification of one or more function of a G-CSF molecule. For example, an external loop may provide sites for the addition of one or more polymer which serves to increase serum half-life, such as a polyethylene glycol molecule. Such polyethylene glycol molecule(s) may be added wherein said loop is altered to include additional lysines which have reactive side groups to which polyethylene glycol moieties are capable of attaching. Other classes of chemical moieties may also be attached to one or more external loops, including but not limited to other biologically active molecules, such as receptors, other therapeutic proteins (such as other hematopoietic factors which would engender a hybrid molecule), or cytotoxic agents (such as diphtheria toxin). This list is of course not complete; one skilled in the art possessed of the desired chemical moiety will have the means to effect attachment of said desired moiety to the desired external loop. Therefore, another class of the present G-CSF analogs includes those with at least one alteration in an external loop wherein said alteration provides for the addition of a chemical moiety such as at least one polyethylene glycol molecule.

Deletions, such as deletions of sites recognized by proteins for degradation of the molecule, may also be effectual in the external loops. This provides alternative means for increasing half-life of a molecule otherwise having the G-CSF receptor binding and signal transduction capabilities (i.e., the ability to selectively stimulate the maturation of neutrophils). Therefore, another class of the present G-CSF analogs

includes those with at least one alteration in an external loop wherein said alteration decreases the turnover of said analog by proteases. Preferred loops for such alterations are the AB loop and the CD loop. One may prepare an abbreviated G-CSF molecule by deleting a portion of the amino acid residues found in the external loops (identified in more detail below), said abbreviated G-CSF molecule may have additional advantages in preparation or in biological function.

Another example relates to the relative charges between amino acid residues which are in proximity to each other. As noted above, the G-CSF molecule contains a relatively tightly packed four helical bundle. Some of the faces on the helices face other helices. At the point (such as a residue) where a helix faces another helix, the two amino acid moieties which face each other may have the same charge, and thus tend to repel each other, which lends instability to the overall molecule. This may be eliminated by changing the charge (to an opposite charge or a neutral charge) of one or both of the amino acid moieties so that there is no repelling. Therefore, another class of G-CSF analogs includes those G-CSF analogs having been altered to modify instability due to surface interactions, such as electron charge location.

In another aspect, the present invention relates to methods for designing G-CSF analogs and related compositions and the products of those methods. The end products of the methods may be the G-CSF analogs as defined above or related compositions. For instance, the examples disclosed herein demonstrate (a) the effects of changes in the constituents (i.e., chemical moieties) of the G-CSF molecule on the G-CSF structure and (b) the effects of changes in structure on biological function. Essentially, therefore, another

aspect of the present invention is a method for preparing a G-CSF analog comprising the steps of:

(a) viewing information conveying the three dimensional structure of a G-CSF molecule wherein the chemical moieties, such as each amino acid residue or each atom of each amino acid residue, of the G-CSF molecule are correlated with said structure;

(b) selecting from said information a site on a G-CSF molecule for alteration;

(c) preparing a G-CSF analog molecule having such alteration; and

(d) optionally, testing such G-CSF analog molecule for a desired characteristic.

One may use the here provided computer programs for a computer-based method for preparing a G-CSF analog. Another aspect of the present invention is therefore a computer based method for preparing a G-CSF analog comprising the steps of:

(a) providing computer expression of the three dimensional structure of a G-CSF molecule wherein the chemical moieties, such as each amino acid residue or each atom of each amino acid residue, of the G-CSF molecule are correlated with said structure;

(b) selecting from said computer expression a site on a G-CSF molecule for alteration;

(c) preparing a G-CSF molecule having such alteration; and

(d) optionally, testing such G-CSF molecule for a desired characteristic.

More specifically, the present invention provides a method for preparing a G-CSF analog comprising the steps of:

(a) viewing the three dimensional structure of a G-CSF molecule via a computer, said computer programmed (i) to express the coordinates of a G-CSF molecule in three dimensional space, and (ii) to allow

for entry of information for alteration of said G-CSF expression and viewing thereof;

(b) selecting a site on said visual image of said G-CSF molecule for alteration;

(c) entering information for said alteration on said computer;

(d) viewing a three dimensional structure of said altered G-CSF molecule via said computer;

(e) optionally repeating steps (a)-(e);

(f) preparing a G-CSF analog with said alteration; and

(g) optionally testing said G-CSF analog for a desired characteristic.

In another aspect, the present invention relates to methods of using the present G-CSF analogs and related compositions and methods for the treatment or protection of mammals, either alone or in combination with other hematopoietic factors or drugs in the treatment of hematopoietic disorders. It is contemplated that one aspect of designing G-CSF analogs will be the goal of enhancing or modifying the characteristics non-modified G-CSF is known to have.

For example, the present analogs may possess enhanced or modified activities, so, where G-CSF is useful in the treatment of (for example) neutropenia, the present compositions and methods may also be of such use.

Another example is the modification of G-CSF for the purpose of interacting more effectively when used in combination with other factors particularly in the treatment of hematopoietic disorders. One example of such combination use is to use an early-acting hematopoietic factor (i.e., a factor which acts earlier in the hematopoiesis cascade on relatively undifferentiated cells) and either simultaneously or in seriatim use of a later-acting hematopoietic factor,

such as G-CSF or analog thereof (as G-CSF acts on the CFU-GM lineage in the selective stimulation of neutrophils). The present methods and compositions may be useful in therapy involving such combinations or "cocktails" of hematopoietic factors.

The present compositions and methods may also be useful in the treatment of leukopenia, mylogenous leukemia, severe chronic neutropenia, aplastic anemia, glycogen storage disease, mucosistitis, and other bone marrow failure states. The present compositions and methods may also be useful in the treatment of hematopoietic deficits arising from chemotherapy or from radiation therapy. The success of bone marrow transplantation, or the use of peripheral blood progenitor cells for transplantation, for example, may be enhanced by application of the present compositions (proteins or nucleic acids for gene therapy) and methods. The present compositions and methods may also be useful in the treatment of infectious diseases, such in the context of wound healing, burn treatment, bacteremia, septicemia, fungal infections, endocarditis, osteopyelitis, infection related to abdominal trauma, infections not responding to antibiotics, pneumonia and the treatment of bacterial inflammation may also benefit from the application of the present compositions and methods. In addition, the present compositions and methods may be useful in the treatment of leukemia based upon a reported ability to differentiate leukemic cells. Welte et al., PNAS-USA 82: 1526-1530 (1985). Other applications include the treatment of individuals with tumors, using the present compositions and methods, optionally in the presence of receptors (such as antibodies) which bind to the tumor cells. For review articles on therapeutic applications, see Lieshhke and Burgess, N.Engl.J.Med. 327: 28-34 and 99-106 (1992) both of which are herein incorporated by reference.

The present compositions and methods may also be useful to act as intermediaries in the production of other moieties; for example, G-CSF has been reported to influence the production of other hematopoietic factors and this function (if ascertained) may be enhanced or modified via the present compositions and/or methods.

The compositions related to the present G-CSF analogs, such as receptors, may be useful to act as an antagonist which prevents the activity of G-CSF or an analog. One may obtain a composition with some or all of the activity of non-altered G-CSF or a G-CSF analog, and add one or more chemical moieties to alter one or more properties of such G-CSF or analog. With knowledge of the three dimensional conformation, one may forecast the best geographic location for such chemical modification to achieve the desired effect.

General objectives in chemical modification may include improved half-life (such as reduced renal, immunological or cellular clearance), altered bioactivity (such as altered enzymatic properties, dissociated bioactivities or activity in organic solvents), reduced toxicity (such as concealing toxic epitopes, compartmentalization, and selective biodistribution), altered immunoreactivity (reduced immunogenicity, reduced antigenicity or adjuvant action), or altered physical properties (such as increased solubility, improved thermal stability, improved mechanical stability, or conformational stabilization). See Francis, *Focus on Growth Factors* 3: 4-10 (May 1992) (published by Mediscript, Mountview Court, Friern Barnet Lane, London N20 OLD, UK).

The examples below are illustrative of the present invention and are not intended as a limitation. It is understood that variations and modifications will occur to those skilled in the art, and it is intended that the appended claims cover all such equivalent

variations which come within the scope of the invention as claimed.

Detailed Description of the Drawings

FIGURE 1 is an illustration of the amino acid sequence of the 174 amino acid species of G-CSF with an additional N-terminal methionine (Seq. ID No.: 1) (Seq. ID No.: 2).

FIGURE 2 is an topology diagram of the crystalline structure of G-CSF, as well as hGH, pGH, GM-CSF, INF-B, IL-2, and IL-4. These illustrations are based on inspection of cited references. The length of secondary structural elements are drawn in proportion to the number of residues. A, B, C, and D helices are labeled according to the scheme used herein for G-CSF. For INF-ß, the original labeling of helices is indicated in parentheses.

FIGURE 3 is an "ribbon diagram" of the three dimensional structure of G-CSF. Helix A is amino acid residues 11-39 (numbered according to Figure 1, above), helix B is amino acid residues 72-91, helix C is amino acid residues 100-123, and helix D is amino acid residues 143-173. The relatively short 3^{10} helix is at amino acid residues 45-48, and the alpha helix is at amino acid residues 48-53. Residues 93-95 form almost one turn of a left handed helix.

FIGURE 4 is a "barrel diagram" of the three dimensional structure of G-CSF. Shown in various shades of gray are the overall cylinders and their orientations for the three dimensional structure of G-CSF. The numbers indicate amino acid residue position according to FIGURE 1 above.

FIGURE 5 is a list of the coordinates used to generate a computer-aided visual image of the three-dimensional structure of G-CSF. The coordinates are set forth below. The columns correspond to separate field:

(i) Field 1 (from the left hand side) is the atom,

(ii) Field 2 is the assigned atom number,

(iii) Field 3 is the atom name (according to the periodic table standard nomenclature, with CB being carbon atom Beta, CG is Carbon atom Gamma, etc.);

(iv) Field 4 is the residue type (according to three letter nomenclature for amino acids as found in, e.g., Stryer, Biochemistry, 3d Ed., W.H. Freeman and Company, N.Y. 1988, inside back cover);

(v) Fields 5-7 are the x-axis, y-axis and z-axis positions of the atom;

(vi) Field 8 (often a "1.00") designates occupancy at that position;

(vii) Field 9 designates the B-factor;

(viii) Field 10 designates the molecule designation. Three molecules (designated a, b, and c) of G-CSF crystallized together as a unit. The designation a, b, or c indicates which coordinates are from which molecule. The number after the letter (1, 2, or 3) indicates the assigned amino acid residue position, with molecule A having assigned positions 10-175, molecule B having assigned positions 210-375, and molecule C having assigned positions 410-575. These positions were so designated so that there would be no overlap among the three molecules which crystallized together. (The "W" designation indicates water).

FIGURE 6 is a schematic representation of the strategy involved in refining the crystallization matrix for parameters involved in crystallization. The crystallization matrix corresponds to the final concentration of the components (salts, buffers and precipitants) of the crystallization solutions in the wells of a 24 well tissue culture plate. These concentrations are produced by pipetting the appropriate volume of stock solutions into the wells of the

microtiter plate. To design the matrix, the crystallographer decides on an upper and lower concentration of the component. These upper and lower concentrations can be pipetted along either the rows (e.g., A1-A6, B1-B6, C1-C6 or D1-D6) or along the entire tray (A1-D6). The former method is useful for checking reproducibility of crystal growth of a single component along a limited number of wells, whereas the later method is more useful in initial screening. The results of several stages of refinement of the crystallization matrix are illustrated by a representation of three plates. The increase in shading in the wells indicates a positive crystallization result which, in the final stages, would be X-ray quality crystals but in the initial stages could be oil droplets, granular precipitates or small crystals approximately less than 0.05 mm in size. Part A represents an initial screen of one parameter in which the range of concentration between the first well (A1) and last well (D6) is large and the concentration increase between wells is calculated as ((concentration A1)-(concentration D6))/23). Part B represents that in later stages of the crystallization matrix refinement of the concentration spread between A1 and D6 would be reduced which would result in more crystals formed per plate. Part C indicates a final stage of matrix refinement in which quality crystals are found in most wells of the plate.

Detailed Description of the Invention

The present invention grows out of the discovery of the three dimensional structure of G-CSF. This three dimensional structure has been expressed via computer program for stereoscopic viewing. By viewing this stereoscopically, structure-function relationships identified and G-CSF analogs have been designed and made.

The Overall Three Dimensional Structure of G-CSF

The G-CSF used to ascertain the structure was a non-glycosylated 174 amino acid species having an extra N-terminal methionine residue incident to bacterial expression. The DNA and amino acid sequence of this G-CSF are illustrated in FIGURE 1.

Overall, the three dimensional structure of G-CSF is predominantly helical, with 103 of the 175 residues forming a 4-alpha-helical bundle. The only other secondary structure is found in the loop between the first two long helices where a 4 residue 3^{10} helix is immediately followed by a 6 residue alpha helix. As shown in FIGURE 2, the overall structure has been compared with the structure reported for other proteins: growth hormone (Abdel-Meguid et al., PNAS-USA 84: 6434 (1987) and Vos et al., Science 255: 305-312 (1992)), granulocyte macrophage colony stimulating factor (Diederichs et al., Science 254: 1779-1782 (1991), interferon-ß (Senda et al., EMBO J. 11: 3193-3201 (1992)), interleukin-2 (McKay Science 257: 1673-1677 (1992)) and interleukin-4 (Powers et al., Science 256: 1673-1677 (1992), and Smith et al., J. Mol. Biol. 224: 899-904 (1992)). Structural similarity among these growth factors occurs despite the absence of similarity in their amino acid sequences.

Presently, the structural information was correlation of G-CSF biochemistry, and this can be

summarized as follows (with sequence position 1 being at the N-terminus):

Sequence Position	Description of Structure	Analysis
1-10	Extended chain	Deletion causes no loss of biological activity
Cys 18	Partially buried	Reactive with DTNB and Thimersososl but not with iodo-acetate
34	Alternative splice site	Insertion reduces biological activity
20-47 (inclusive)	Helix A, first disulfide and portion of AB helix	Predicted receptor binding region based on neutralizing antibody data
20, 23, 24	Helix A	Single alanine mutation of residue(s) reduces biological activity. Predicted receptor binding (Site B).
165-175 (inclusive)	Carboxy terminus	Deletion reduces biological activity

This biochemical information, having been gleaned from antibody binding studies, see Layton et al., Biochemistry 266: 23815-23823 (1991), was superimposed on the three-dimensional structure in order to design G-CSF analogs. The design, preparation, and testing of these G-CSF analogs is described in Example 1 below.

EXAMPLE 1

This Example describes the preparation of crystalline G-CSF, the visualization of the three dimensional structure of recombinant human G-CSF via

computer-generated image, the preparation of analogs, using site-directed mutagenesis or nucleic acid amplification methods, the biological assays and HPLC analysis used to analyze the G-CSF analogs, and the resulting determination of overall structure/function relationships. All cited publications are herein incorporated by reference.

A. Use of Automated Crystallization

The need for a three-dimensional structure of recombinant human granulocyte colony stimulating factor (r-hu-G-CSF), and the availability of large quantities of the purified protein, led to methods of crystal growth by incomplete factorial sampling and seeding. Starting with the implementation of incomplete factorial crystallization described by Jancarik and Kim, J. Appl. Crystallogr. 24: 409 (1991) solution conditions that yielded oil droplets and birefringence aggregates were ascertained. Also, software and hardware of an automated pipetting system were modified to produce some 400 different crystallization conditions per day. Weber, J. Appl. Crystallogr. 20: 366-373 (1987). This procedure led to a crystallization solution which produced r-hu-G-CSF crystals.

The size, reproducibility and quality of the crystals was improved by a seeding method in which the number of "nucleation initiating units" was estimated by serial dilution of a seeding solution. These methods yielded reproducible growth of 2.0 mm r-hu-G-CSF crystals. The space group of these crystals is $P2_12_12_1$ with cell dimensions of a=90 Å, b=110 Å and c=49 Å, and they diffract to a resolution of 2.0 Å.

1. Overall Methodology

To search for the crystallizing conditions of a new protein, Carter and Carter, J. Biol. Chem. 254:

122219-12223 (1979) proposed the incomplete factorial method. They suggested that a sampling of a large number of randomly selected, but generally probable, crystallizing conditions may lead to a successful combination of reagents that produce protein crystallization. This idea was implemented by Jancarik and Kim, J. Appl. Crystallogr. 24: 409(1991), who described 32 solutions for the initial crystallization trials which cover a range of pH, salts and precipitants. Here we describe an extension of their implementation to an expanded set of 70 solutions. To minimize the human effort and error of solution preparation, the method has been programmed for an automatic pipetting machine.

Following Weber's method of successive automated grid searching (SAGS), J.Cryst. Growth 90: 318-324(1988), the robotic system was used to generate a series of solutions which continually refined the crystallization conditions of temperature, pH, salts and precipitant. Once a solution that could reproducibly grow crystals was determined, a seeding technique which greatly improved the quality of the crystals was developed. When these methods were combined, hundreds of diffraction quality crystals (crystals diffracting to at least about 2.5 Angstroms, preferably having at least portions diffracting to below 2 Angstroms, and more preferably, approximately 1 Angstrom) were produced in a few days.

Generally, the method for crystallization, which may be used with any protein one desires to crystallize, comprises the steps of:

(a) combining aqueous aliquots of the desired protein with either (i) aliquots of a salt solution, each aliquot having a different concentration of salt; or (ii) aliquots of a precipitant solution, each aliquot having a different concentration of precipitant,

optionally wherein each combined aliquot is combined in the presence of a range of pH;

(b) observing said combined aliquots for precrystalline formations, and selecting said salt or precipitant combination and said pH which is efficacious in producing precrystalline forms, or, if no precrystalline forms are so produced, increasing the protein starting concentration of said aqueous aliquots of protein;

(c) after said salt or said precipitant concentration is selected, repeating step (a) with said previously unselected solution in the presence of said selected concentration; and

(d) repeating step (b) and step (a) until a crystal of desired quality is obtained.

The above method may optionally be automated, which provides vast savings in time and labor. Preferred protein starting concentrations are between 10mg/ml and 20mg/ml, however this starting concentration will vary with the protein (the G-CSF below was analyzed using 33mg/ml). A preferred range of salt solution to begin analysis with is (NaCl) of 0-2.5M. A preferred precipitant is polyethylene glycol 8000, however, other precipitants include organic solvents (such as ethanol), polyethylene glycol molecules having a molecular weight in the range of 500-20,000, and other precipitants known to those skilled in the art. The preferred pH range is pH 4.5 , 5.0, 5.5, 6.0, 6.5, 7.0, 7.5, 8.0, 8.5, and 9.0. Precrystallization forms include oils, birefringement precipitants, small crystals (< approximately 0.05 mm), medium crystals (approximately 0.5 to .5 mm) and large crystals (> approximately 0.5 mm). The preferred time for waiting to see a crystalline structure is 48 hours, although weekly observation is also preferred, and generally, after about one month, a different protein

concentration is utilized (generally the protein concentration is increased). Automation is preferred, using the Accuflex system as modified. The preferred automation parameters are described below.

Generally, protein with a concentration between 10 mg/ml and 20 mg/ml was combined with a range of NaCl solutions from 0-2.5 M, and each such combination was performed (separately) in the presence of the above range of concentrations. Once a precrystallization structure is observed, that salt concentration and pH range are optimized in a separate experiment, until the desired crystal quality is achieved. Next, the precipitant concentration, in the presence of varying levels of pH is also optimized. When both are optimized, the optimal conditions are performed at once to achieve the desired result (this is diagrammed in FIGURE 6).

a. Implementation of an automated pipetting system

Drops and reservoir solutions were prepared by an Accuflex pipetting system (ICN Pharmaceuticals, Costa Mesa, CA) which is controlled by a personal computer that sends ASCII codes through a standard serial interface. The pipetter samples six different solutions by means of a rotating valve and pipettes these solutions onto a plate whose translation in a x-y coordinate system can be controlled. The vertical component of the system manipulates a syringe that is capable both of dispensing and retrieving liquid.

The software provided with the Accuflex was based on the SAGS method as proposed by Cox and Weber, J.Appl. Crystallogr. 20: 366-373 (1987). This method involves the systematic variation of two major crystallization parameters, pH and precipitant concentration, with provision to vary two others. While

building on these concepts, the software used here provided greater flexibility in the design and implementation of the crystallization solutions used in the automated grid searching strategy. As a result of this flexibility the present software also created a larger number of different solutions. This is essential for the implementation of the incomplete factorial method as described in that section below.

To improve the speed and design of the automated grid searching strategy, the Accuflex pipetting system required software and hardware modifications. The hardware changes allowed the use of two different micro-titer trays, one used for handing drop and one used for sitting drop experiments, and a Plexiglas tray which held 24 additional buffer, salt and precipitant solutions. These additional solutions expanded the grid of crystallizing conditions that could be surveyed.

To utilize the hardware modifications, the pipetting software was written in two subroutines; one subroutine allows the crystallographer to design a matrix of crystallization solutions based on the concentrations of their components and the second subroutine to translate these concentrations into the computer code which pipettes the proper volumes of the solutions into the crystallization trays. The concentration matrices can be generated by either of two programs. The first program (MRF, available from Amgen, Inc., Thousand Oaks, CA) refers to a list of stock solution concentrations supplied by the crystallographer and calculates the required volume to be pipette to achieve the designated concentration. The second method, which is preferred, incorporates a spread sheet program (Lotus) which can be used to make more sophisticated gradients of precipitants or pH. The concentration matrix created by either program is

interpreted by the control program (SUX, a modification of the program found in the Accuflex pipetter originally and available from Amgen, Inc., Thousand Oaks, CA) and the wells are filled accordingly.

b. Implementation of the Incomplete Factorial Method

The convenience of the modified pipetting system for preparing diverse solutions improved the implementation of an expanded incomplete factorial method. The development of a new set of crystallization solutions having "random" components was generated using the program INFAC, Carter et al., J.Cryst. Growth 90: 60-73(1988) which produced a list containing 96 random combinations of one factor from three variables. Combinations of calcium and phosphate which immediately precipitated were eliminated, leaving 70 distinct combinations of precipitants, salts and buffers. These combinations were prepared using the automated pipetter and incubated for 1 week. The mixtures were inspected and solutions which formed precipitants were prepared again with lower concentrations of their components. This was repeated until all wells were clear of precipitant.

c. Crystallization of r-hu-G-CSF

Several different crystallization strategies were used to find a solution which produced x-ray quality crystals. These strategies included the use of the incomplete factorial method, refinement of the crystallization conditions using successive automated grid searches (SAGS), implementation of a seeding technique and development of a crystal production procedure which yielded hundreds of quality crystals overnight. Unless otherwise noted the screening and production of r-hu-G-CSF crystals utilized the hanging drop vapor diffusion method. Afinsen et al., Physical

principles of protein crystallization. In: Eisenberg (ed.), Advances in Protein Chemistry 41: 1-33 (1991).

The initial screening for crystallization conditions of r-hu-G-CSF used the Jancarik and Kim, J.Appl.Crystallogr. 24: 409(1991) incomplete factorial method which resulted in several solutions that produced "precrystallization" results. These results included birefringent precipitants, oils and very small crystals (< .05 mm). These precrystallizations solutions then served as the starting points for systematic screening.

The screening process required the development of crystallization matrices. These matrices corresponded to the concentration of the components in the crystallization solutions and were created using the IBM-PC based spread sheet Lotus™ and implemented with the modified Accuflex pipetting system. The strategy in designing the matrices was to vary one crystallization condition (such as salt concentration) while holding the other conditions such as pH, and precipitant concentration constant. At the start of screening, the concentration range of the varied condition was large but the concentration was successively refined until all wells in the micro-titer tray produced the same crystallization result. These results were scored as follows: crystals, birefringement precipitate, granular precipitate, oil droplets and amorphous mass. If the concentration of a crystallization parameter did not produce at least a precipitant, the concentration of that parameter was increased until a precipitant formed. After each tray was produced, it was left undisturbed for at least two days and then inspected for crystal growth. After this initial screening, the trays were then inspected on a weekly basis.

From this screening process, two independent solutions with the same pH and precipitant but differing in salts (MgCl, $LiSO_4$) were identified which produced

small (0.1 x 0.05 x 0.05 mm) crystals. Based on these results, a new series of concentration matrices were produced which varied MgCl with respect to $LiSO_4$ while keeping the other crystallization parameters constant. This series of experiments resulted in identification of a solution which produced diffraction quality crystals (> approximately 0.5 mm) in about three weeks. To find this crystallization growth solution (100 mM Mes pH 5.8, 380 mM $MgCl_2$, 220 mM LiSO4 and 8% PEG 8k) approximately 8,000 conditions had been screened which consumed about 300 mg of protein.

The size of the crystals depended on the number of crystals forming per drop. Typically 3 to 5 crystals would be formed with average size of (1.0 x 0.7 x 0.7 mm). Two morphologies which had an identical space group ($P2_12_12_1$) and unit cell dimensions a=90.2, b=110.2, c=49.5 were obtained depending on whether or not seeding (see below) was implemented. Without seeding, the r-hu-G-CSF crystals had one long flat surface and rounded edges.

When seeding was employed, crystals with sharp faces were observed in the drop within 4 to 6 hours (0.05 by 0.05 by 0.05 mm). Within 24 hours, crystals had grown to (0.7 by 0.7 by 0.7 mm) and continued to grow beyond 2 mm depending on the number of crystals forming in the drop.

d. Seeding and determination of nucleation initiation sites.

The presently provided method for seeding crystals establishes the number of nucleation initiation units in each individual well used (here, after the optimum conditions for growing crystals had been determined). The method here is advantageous in that the number of "seeds" affects the quality of the crystals, and this in turn affects the degree of resolution. The present seeding here also provides

advantages in that with seeding, G-CSF crystal grows in a period of about 3 days, whereas without seeding, the growth takes approximately three weeks.

In one series of production growth (see methods), showers of small but well defined crystals were produced overnight (<0.01 x 0.01 x0.01 mm). Crystallization conditions were followed as described above except that a pipette tip employed in previously had been reused. Presumably, the crystal showering effect was caused by small nucleation units which had formed in the used tip and which provided sites of nucleation for the crystals. Addition of a small amount (0.5 ul) of the drops containing the crystal showers to a new drop under standard production growth conditions resulted in a shower of crystals overnight. This method was used to produce several trays of drops containing crystal showers which we termed "seed stock".

The number of nucleation initiation units (NIU) contained within the "seed stock" drops was estimated to attempt to improve the reproducibility and quality of the r-hu-GCSF crystals. To determine the number of NIU in the "seed stock", an aliquot of the drop was serially diluted along a 96 well microtiter plate. The microtiter plate was prepared by adding 50 ul of a solution containing equal volumes of r-hu-G-CSF (33 mg/ml) and the crystal growth solution (described above) in each well. An aliquot (3 ul) of one of the "seed stock" drops was transferred to the first well of the microtiter plate. The solution in the well was mixed and 3 ul was then transferred to the next well along the row of the microtiter plate. Each row of the microtiter plate was similarly prepared and the tray was sealed with plastic tape. Overnight, small crystals formed in the bottom of the wells of the microtiter plate and the number of crystals in the wells were correlated to the dilution of the original "seed stock".

To produce large single crystals, the "seed stock" drop was appropriately diluted into fresh CGS and then an aliquot of this solution containing the NIU was transferred to a drop

Once crystallization conditions had been optimized, crystals were grown in a production method in which 3 ml each of CGS and r-hu-G-CSF (33 mg/ml) were mixed to create 5 trays (each having 24 wells). This method included the production of the refined crystallization solution in liter quantities, mixing this solution with protein and placing the protein/crystallization solution in either hanging drop or sitting drop trays. This process typically yielded 100 to 300 quality crystals (>0.5 mm) in about 5 days.

e. Experimental Methods

Materials

Crystallographic information was obtained starting with r-hu-met-G-CSF with the amino acid sequence as provided in FIGURE 1 with a specific activity of 1.0 +/- 0.6 x 10^8U/mg (as measured by cell mitogenesis assay in a 10 mM acetate buffer at pH 4.0 (in Water for Injection) at a concentration of approximately 3 mg/ml solution was concentrated with an Amicon concentrator at 75 psi using a YM10 filter. The solution was typically concentrated 10 fold at 4°C and stored for several months.

Initial Screening

Crystals suitable for X-ray analysis were obtained by vapor-diffusion equilibrium using hanging drops. For preliminary screening, 7 ul of the protein solution at 33 mg/ml (as prepared above) was mixed with an equal volume of the well solution, placed on siliconized glass plates and suspended over the well solution utilizing Linbro tissue culture plates (Flow Laboratories, McLean, Va). All of the pipetting was performed with the Accuflex pipetter, however, trays

were removed from the automated pipetter after the well solutions had been created and thoroughly mixed for at least 10 minutes with a table top shaker. The Linbro trays were then returned to the pipetter which added the well and protein solutions to the siliconized cover slips. The cover slips were then inverted and sealed over 1 ml of the well solutions with silicon grease.

The components of the automated crystallization system are as follows. A PC-DOS computer system was used to design a matrix of crystallization solutions based on the concentration of their components. These matrices were produced with either MRF of the Lotus spread sheet (described above). The final product of these programs is a data file. This file contains the information required by the SUX program to pipette the appropriate volume of the stock solutions to obtain the concentrations described in the matrices. The SUX program information was passed through a serial I/O port and used to dictate to the Accuflex pipetting system the position of the valve relative to the stock solutions, the amount of solution to be retrieved, and then pipetted into the wells of the microtiter plates and the X-Y position of each well (the column/row of each well). Addition information was transmitted to the pipetter which included the Z position (height) of the syringe during filling as well as the position of a drain where the system pauses to purge the syringe between fillings of different solutions. The 24 well microtiter plate (either Linbro or Cryschem) and cover slip holder was placed on a plate which was moved in the X-Y plane. Movement of the plate allowed the pipetter to position the syringe to pipette into the wells. It also positioned the coverslips and vials and extract solutions from these sources. Prior the pipetting, the Linbro microtiter plates had a thin film of grease applied around the edges of the wells.

After the crystallization solutions were prepared in the wells and before they were transferred to the cover slips, the microtiter plate was removed from the pipetting system, and solutions were allowed to mix on a table top shaker for ten minutes. After mixing, the well solution was either transferred to the cover slips (in the case of the hanging drop protocol) or transferred to the middle post in the well (in the case of the sitting drop protocol). Protein was extracted from a vial and added to the coverslip drop containing the well solution (or to the post). Plastic tape was applied to the top of the Cryschem plate to seal the wells.

Production Growth

Once conditions for crystallization had been optimized, crystal growth was performed utilizing a "production" method. The crystallization solution which contained 100 mM Mes pH 5.8, 380 mM MgCl2, 220 mM LiSO4, and 8% PEG 8K was made in 1 liter quantities. Utilizing an Eppindorf syringe pipetter, 1 ml aliquots of this solution were pipetted into each of the wells of the Linbro plate. A solution containing 50% of this solution and 50% G-CSF (33 mg/ml) was mixed and pipetted onto the siliconized cover slips. Typical volumes of these drops were between 50 and 100 ul and because of the large size of these drops, great care was taken in flipping the coverslips and suspending the drops over the wells.

Data Collection

The structure has been refined with X-PLOR (Bruniger, X-PLOR version 3.0, A system for crystallography and NMR, Yale University, New Haven CT) against 2.2Å data collected on an R-AXIS (Molecular Structure, Corp. Houston, TX) imaging plate detector.

f. Observations

As an effective recombinant human therapeutic, r-hu-G-CSF has been produced in large quantities and gram levels have been made available for structural analysis. The crystallization methods provided herein are likely to find other applications as other proteins of interest become available. This method can be applied to any crystallographic project which has large quantities of protein (approximately >200 mg). As one skilled in the art will recognize, the present materials and methods may be modified and equivalent materials and methods may be available for crystallization of other proteins.

B. Computer Program For Visualizing The Three Dimensional Structure of G-CSF

Although diagrams, such as those in the Figures herein, are useful for visualizing the three dimensional structure of G-CSF, a computer program which allows for stereoscopic viewing of the molecule is contemplated as preferred. This stereoscopic viewing, or "virtual reality" as those in the art sometimes refer to it, allows one to visualize the structure in its three dimensional form from every angle in a wide range of resolution, from macromolecular structure down to the atomic level. The computer programs contemplated herein also allow one to change perspective of the viewing angle of the molecule, for example by rotating the molecule. The contemplated programs also respond to changes so that one may, for example, delete, add, or substitute one or more images of atoms, including entire amino acid residues, or add chemical moieties to existing or substituted groups, and visualize the change in structure.

Other computer based systems may be used; the elements being: (a) a means for entering information, such as orthogonal coordinates or other numerically

assigned coordinates of the three dimensional structure of G-CSF; (b) a means for expressing such coordinates, such as visual means so that one may view the three dimensional structure and correlate such three dimensional structure with the composition of the G-CSF molecule, such as the amino acid composition; (c) optionally, means for entering information which alters the composition of the G-CSF molecule expressed, so that the image of such three dimensional structure displays the altered composition.

The coordinates for the preferred computer program used are presented in FIGURE 5. The preferred computer program is Insight II, version 4, available from Biosym in San Diego, CA. For the raw crystallographic structure, the observed intensities of the diffraction data ("F-obs") and the orthogonal coordinates are also deposited in the Protein Data Bank, Chemistry Department, Brookhaven National Laboratory, Upton, New York 119723, USA and these are herein incorporated by reference.

Once the coordinates are entered into the Insight II program, one can easily display the three dimensional G-CSF molecule representation on a computer screen. The preferred computer system for display is Silicon Graphics 320 VGX (San Diego, CA). For stereoscopic viewing, one may wear eyewear (Crystal Eyes, Silicon Graphics) which allows one to visualize the G-CSF molecule in three dimensions stereoscopically, so one may turn the molecule and envision molecular design.

Thus, the present invention provides a method of designing or preparing a G-CSF analog with the aid of a computer comprising:

(a) providing said computer with the means for displaying the three dimensional structure of a G-CSF molecule including displaying the composition of

moieties of said G-CSF molecule, preferably displaying the three dimensional location of each amino acid, and more preferably displaying the three dimensional location of each atom of a G-CSF molecule;

(b) viewing said display;

(c) selecting a site on said display for alteration in the composition of said molecule or the location of a moiety; and

(d) preparing a G-CSF analog with such alteration.

The alteration may be selected based on the desired structural characteristics of the end-product G-CSF analog, and considerations for such design are described in more detail below. Such considerations include the location and compositions of hydrophobic amino acid residues, particularly residues internal to the helical structures of a G-CSF molecule which residues, when altered, alter the overall structure of the internal core of the molecule and may prevent receptor binding; the location and compositions of external loop structures, alteration of which may not affect the overall structure of the G-CSF molecule.

FIGURES 2-4 illustrate the overall three dimensional conformation in different ways. The topological diagram, the ribbon diagram, and the barrel diagram all illustrate aspects of the conformation of G-CSF.

FIGURE 2 illustrates a comparison between G-CSF and other molecules. There is a similarity of architecture, although these growth factors differ in the local conformations of their loops and bundle geometrics. The up-up-down-down topology with two long crossover connections is conserved, however, among all six of these molecules, despite the dissimilarity in amino acid sequence.

FIGURE 3 illustrates in more detail the secondary structure of recombinant human G-CSF. This ribbon diagram illustrates the handedness of the helices and their positions relative to each other.

FIGURE 4 illustrates in a different way the conformation of recombinant human G-CSF. This "barrel" diagram illustrates the overall architecture of recombinant human G-CSF.

C. Preparation of Analogs Using M13 Mutagenesis

This example relates to the preparation of G-CSF analogs using site directed mutagenesis techniques involving the single stranded bacteriophage M13, according to methods published in PCT Application No. WO 85/00817 (Souza et al., published February 28, 1985, herein incorporated by reference). This method essentially involves using a single-stranded nucleic acid template of the non-mutagenized sequence, and binding to it a smaller oligonucleotide containing the desired change in the sequence. Hybridization conditions allow for non-identical sequences to hybridize and the remaining sequence is filled in to be identical to the original template. What results is a double stranded molecule, with one of the two strands containing the desired change. This mutagenized single strand is separated, and used itself as a template for its complementary strand. This creates a double stranded molecule with the desired change.

The original G-CSF nucleic acid sequence used is presented in FIGURE 1, and the oligonucleotides containing the mutagenized nucleic acid(s) are presented in Table 2. Abbreviations used herein for amino acid residues and nucleotides are conventional, see Stryer, Biochemistry, 3d Ed., W.H. Freeman and Company, N.Y., N.Y. 1988, inside back cover.

The original G-CSF nucleic acid sequence was first placed into vector M13mp21. The DNA from single stranded phage M13mp21 containing the original G-CSF sequence was then isolated, and resuspended in water. For each reaction, 200 ng of this DNA was mixed with a 1.5 pmole of phosphorylated oligonucleotide (Table 2) and suspended in 0.1M Tris, 0.01M $MgCl_2$, 0.005M DTT, 0.1mM ATP, pH 8.0. The DNAs were annealed by heating to 65°C and slowly cooling to room temperature.

Once cooled, 0.5mM of each ATP, dATP, dCTP, dGTP, TTP, 1 unit of T4 DNA ligase and 1 unit of Klenow fragment of E. coli polymerase 1 were added to the 1 unit of annealed DNA in 0.1M Tris, 0.025M NaCl, 0.01M $MgCl_2$, 0.01M DTT, pH 7.5.

The now double stranded, closed circular DNA was used to transfect E. coli without further purification. Plaques were screened by lifting the plaques with nitrocellulose filters, and then hybridizing the filters with single stranded DNA end-labeled with P^{32} for 1 hour at 55-60°C. After hybridization, the filters were washed at 0-3°C below the melt temperature of the oligo (2°C for A-T, 4°C for G-C) which selectively left autoradiography signals corresponding to plaques with phage containing the mutated sequence. Positive clones were confirmed by sequencing.

Set forth below are the oligonucleotides used for each G-CSF analog prepared via the M13 mutagenesis method. The nomenclature indicates the residue and the position of the original amino acid (e.g., Lysine at position 17), and the residue and position of the substituted amino acid (e.g., arginine 17). A substitution involving more than one residue is indicated via superscript notation, with commas between the noted positions or a semicolon indicating different residues. Deletions with no substitutions are so noted.

The oligonucleotide sequences used for M13-based mutagenesis are next indicated; these oligonucleotides were manufactured synthetically, although the method of preparation is not critical, any nucleic acid synthesis method and/or equipment may be used. The length of the oligo is also indicated. As indicated above, these oligos were allowed to contact the single stranded phage vector, and then single nucleotides were added to complete the G-CSF analog nucleic acid sequence.

Table 2

G-CSF ANALOGS	SEQUENCES (5'-> 3')	Length (nucleotide)	Seq. ID
Lys^{17}->Arg^{17}	CTT TCT GCT GCG TTG TCT GGA ACA	24	3
Lys^{24}->Arg^{24}	ACA GGT TCG TCG TAT CCA GGG TG	23	4
Lys^{35}->Arg^{35}	CAC TGC AAG AAC GTC TGT GCG CT	23	5
Lys^{41}->Arg^{41}	CGC TAC TTA CCG TCT GTG CCA TC	23	6
$Lys^{17,24,35}$-> $Arg^{17,24,35}$	CTT TCT GCT GCG TTG TCT GGA ACA	24	7
	ACA GGT TCG TCG TAT CCA GGG TG	23	8
	CAC TGC AAG AAC GTC TGT GCG CT	23	9
$Lys^{17,24,41}$-> $Arg^{17,24,41}$	CTT TCT GCT GCG TTG TCT GGA ACA	24	10
	ACA GGT TCG TCG TAT CCA GGG TG	23	11
	CGC TAC TTA CCG TCT GTC CCA TC	23	12
$Lys^{17,35,41}$-> $Arg^{17,35,41}$	CTT TCT GCT GCG TTG TCT GGA ACA	24	13
	CAC TGC AAG AAC GTC TGT GCG CT	23	14
	CGC TAC TTA CCG TCT GTG CCA TC	23	15
$Lys^{24,35,41}$-> $Arg^{24,35,41}$	ACA GGT TCG TCG TAT CCA GGG TG	23	16
	CAC TGC AAG AAC GTC TGT GCG CT	23	17
	CGC TAC TTA CCG TCT GTG CCA TC	23	18

Table 2 (con't)

G-CSF ANALOGS	SEQUENCES (5'-> 3')	Length (nucleotide)	Seq. ID
$Lys^{17,24,35,41}$-> $Arg^{17,24,35,41}$	CTT TCT GCT GCG TTG TCT GGA ACA	24	19
	ACA GGT TCG TCG TAT CCA GGG TG	23	20
	CAC TGC AAG AAC GTC TGT GCG CT	23	21
	CGC TAC TTA CCG TCT GTG CCA TC	23	22
Cys^{18}->Ala^{18}	TCT GCT GAA AGC TCT GGA ACA GG	23	23
Gln^{68}->Glu^{68}	CTT GTC CAT CTG AAG CTC TTC AG	23	24
$Cys^{37,43}$-> $Ser^{37,43}$	GAA AAA CTG TCC GCT ACT TAC AAA CTG TCC CAT CCG G	37	25
Gln^{26}->Ala^{26}	TTC GTA AAA TCG CGG GTG ACG G	22	26
Gln^{174}->Ala^{174}	TCA TCT GGC TGC GCC GTA ATA G	22	27
Arg^{170}->Ala^{170}	CCG TGT TCT GGC TCA TCT GGC T	22	28
Arg^{167}->Ala^{167}	GAA GTA TCT TAC GCT GTT CTG CGT	24	29
Deletion 167	GAA GTA TCT TAC TAA GTT CTG CGT C	25	30
Lys^{41}->Ala^{41}	CGC TAC TTA CGC ACT GTG CCA T	22	31
His^{44}->Lys^{44}	CAA ACT GTG CAA GCC GGA AGA G	22	32
Glu^{47}->Ala^{47}	CAT CCG GAA GCA CTG GTA CTG C	22	33

Table 2 (con't)

G-CSF ANALOGS	SEQUENCES (5'-> 3')	Length (nucleotide)	Seq. ID
Arg^{23}->Ala^{23}	GGA ACA GGT TGC TAA AAT CCA GG	23	34
Lys^{24}->Ala^{24}	GAA CAG GTT CGT GCG ATC CAG GGT G	25	35
Glu^{20}->Ala^{20}	GAA ATG TCT GGC ACA GGT TCG T	22	36
Asp^{28}->Ala^{28}	TCC AGG GTG CCG GTG CTG C	19	37
Met^{127}->Glu^{127}	AAG AGC TCG GTG AGG CAC CAG CT	23	38
Met^{138}->Glu^{138}	CTC AAG GTG CTG AGC CGG CAT TC	23	39
Met^{127}->Leu^{127}	GAG CTC GGT CTG GCA CCA GC	20	40
Met^{138}->Leu^{138}	TCA AGG TGC TCT GCC GGC ATT	21	41
Ser^{13}->Ala^{13}	TCT GCC GCA AGC CTT TCT GCT GA	23	42
Lys^{17}->Ala^{17}	CTT TCT GCT GGC ATG TCT GGA ACA	24	43
Gln^{121}->Ala^{121}	CTA TTT GGC AAG CGA TGG AAG AGC	24	44
Glu^{124}->Ala^{124}	CAG ATG GAA GCG CTC GGT ATG	21	45

Table 2 (con't)

G-CSF ANALOGS	SEQUENCES (5'-> 3')	Length (nucleotide)	Seq. ID
$Met^{127,138}$-> $Leu^{127,138}$	GAG CTC GGT CTG GCA CCA GC	20	46
	TCA AGG TGC TCT GCC GGC ATT	21	47
**Glu^{20}->Ala^{20}; Ser^{13}->Gly^{13}	GAA ATG TCT GGC ACA GGT TCG T	22	48

** This analog came about during the preparation of G-CSF analog Glu^{20}->Ala^{20}. As several clones were being sequenced to identify the Glu^{20}->Ala^{20} analog, the Glu^{20}->Ala^{20}; Ser^{13}->Gly^{13} analog was identified. This double mutant was the result of an *in vitro* Klenow DNA polymerase reaction mistake.

D. Preparation of G-CSF Analogs Using DNA Amplification

This example relates to methods for producing G-CSF analogs using a DNA amplification technique. Essentially, DNA encoding each analog was amplified in two separate pieces, combined, and then the total sequence itself amplified. Depending upon where the desired change in the original G-CSF DNA was to be made, internal primers were used to incorporate the change, and generate the two separate amplified pieces. For example, for amplification of the 5' end of the desired analog DNA, a 5' flanking primer (complementary to a sequence of the plasmid upstream from the G-CSF original DNA) was used at one end of the region to be amplified, and an internal primer, capable of hybridizing to the original DNA but incorporating the desired change, was used for priming the other end. The resulting amplified region stretched from the 5' flanking primer through the internal primer. The same was done for the 3' terminus, using a 3' flanking primer (complementary to a sequence of the plasmid downstream from the G-CSF original DNA) and an internal primer complementary to the region of the intended mutation. Once the two "halves" (which may or may not be equal in size, depending on the location of the internal primer) were amplified, the two "halves" were allowed to connect. Once connected, the 5' flanking primer and the 3' flanking primer were used to amplify the entire sequence containing the desired change.

If more than one change is desired, the above process may be modified to incorporate the change into the internal primer, or the process may be repeated using a different internal primer. Alternatively, the gene amplification process may be used with other methods for creating changes in nucleic acid sequence, such as the phage based mutagenesis technique as

described above. Examples of process for preparing analogs with more than one change are described below.

To create the G-CSF analogs described below, the template DNA used was the sequence as in FIGURE 1 plus certain flanking regions (from a plasmid containing the G-CSF coding region). These flanking regions were used as the 5' and 3' flanking primers and are set forth below. The amplification reactions were performed in 40 ul volumes containing 10 mM Tris-HCl, 1.5 mM $MgCl_2$, 50 mM KCl, 0.1 mg/ml gelatin, pH 8.3 at 20°C. The 40 ul reactions also contained 0.1mM of each dNTP, 10 pmoles of each primer, and 1 ng of template DNA. Each amplification was repeated for 15 cycles. Each cycle consisted of 0.5 minutes at 94°C, 0.5 minutes at 50°C, and 0.75 minutes at 72°C. Flanking primers were 20 nucleotides in length and internal primers were 20 to 25 nucleotides in length. This resulted in multiple copies of double stranded DNA encoding either the front portion or the back portion of the desired G-CSF analog.

For combining the two "halves," one fortieth of each of the two reactions was combined in a third DNA amplification reaction. The two portions were allowed to anneal at the internal primer location, as their ends bearing the mutation were complementary, and following a cycle of polymerization, give rise to a full length DNA sequence. Once so annealed, the whole analog was amplified using the 5' and 3' flanking primers. This amplification process was repeated for 15 cycles as described above.

The completed, amplified analog DNA sequence was cleaved with XbaI and XhoI restriction endonuclease to produce cohesive ends for insertion into a vector. The cleaved DNA was placed into a plasmid vector, and that vector was used to transform E. coli. Transformants were challenged with kanamycin at 50 ug/ml and incubated at 30°C. Production of G-CSF analog

protein was confirmed by polyacrylamide gel electrophoresis of a whole cell lysate. The presence of the desired mutation was confirmed by DNA sequence analysis of plasmid purified from the production isolate. Cultures were then grown, and cells were harvested, and the G-CSF analogs were purified as set forth below.

Set forth below in Table 3 are the specific primers used for eachanalog made using gene amplification.

Table 3

Analog Seq. ID	Internal Primer(5'->3')	
His^{44}->Ala^{44}	5'primer-TTCCGGAGCGCACAGTTTG	49
	3'primer-CAAACTGTGGGCTCCGGAAGAGC	50
Thr^{117}->Ala^{117}	5'primer-ATGCCAAATTGCAGTAGCAAAG	51
	3'primer-CTTTGCTACTGCAATTTGGCAACA	52
Asp^{110}->Ala^{110}	5'primer-ATCAGCTACTGCTAGCTGCAGA	53
	3'primer-TCTGCAGCTAGCAGTAGCTGACT	54
Gln^{21}->Ala^{21}	5'primer-TTACGAACCGCTTCCAGACATT	55
	3'primer-AATGTCTGGAAGCGGTTCGTAAAAT	56
Asp^{113}->Ala^{113}	5'primer-GTAGCAAATGCAGCTACATCTA	57
	3'primer-TAGATGTAGCTGCATTTGCTACTAC	58
His^{53}->Ala^{53}	5'primer-CCAAGAGAAGCACCCAGCAG	59
	3'primer-CTGCTGGGTGCTTCTCTTGGGA	60

For each analog, the following 5' flanking primer was used:

5'-CACTGGCGGTGATAATGAGC 61

(Table 3 con't)

For each analog, the following 3' flanking primer was used:

3'-GGTCATTACGGACCGGATC 62

1. Construction of Double Mutation

To make G-CSF analog $Gln^{12,21}$->$Glu^{12,21}$, two separate DNA amplifications were conducted to create the two DNA mutations. The template DNA used was the sequence as in FIGURE 1 plus certain flanking regions (from a plasmid containing the G-CSF coding region). The precise sequences are listed below. Each of the two DNA amplification reactions were carried out using a Perkin Elmer/Cetus DNA Thermal Cycler. The 40 ul reaction mix consisted of 1X PCR Buffer (Cetus), 0.2 mM each of the 4 dXTPs (Cetus), 50 pmoles of each primer oligonucleotide, 2 ng of G-CSF template DNA (on a plasmid vector), and 1 unit of Taq polymerase (Cetus). The amplification process was carried out for 30 cycles. Each cycle consisted of 1minute at 94°C, 2 minutes at 50°C, and 3 minutes at 72°C.

DNA amplification "A" used the oligonucleotides:

5' CCACTGGCGGTGATACTGAGC 3' (Seq. ID 63) and

5' AGCAGAAAGCTTTCCGGCAGAGAAGAAGCAGGA 3' (Seq. ID 64)

DNA amplification "B" used the oligonucleotides:

5' GCCGCAAAGCTTTCTGCTGAAATGTCTGGAAGAGGTTCGTAAAATCCAGGGTGA 3' (Seq. ID 65) and

5' CTGGAATGCAGAAGCAAATGCCGGCATAGCACCTTCAGTCGGTTGCAGAGCTGGTGCCA 3' (Seq. ID 66)

From the 109 base pair double stranded DNA product obtained after DNA amplification "A", a 64 base pair XbaI to HindIII DNA fragment was cut and isolated that contained the DNA mutation Gln^{12}->Glu^{12}. From the 509 base pair double stranded DNA product obtained after DNA amplification "B", a 197 base pair HindIII to BsmI

DNA fragment was cut and isolated that contained the DNA mutation Gln^{21}->Glu^{21}.

The "A" and "B" fragments were ligated together with a 4.8 kilo-base pair XbaI to BsmI DNA plasmid vector fragment. The ligation mix consisted of equal molar DNA restriction fragments, ligation buffer (25 mM Tris-HCl pH 7.8, 10 mM $MgCl_2$, 2 mM DTT, 0.5 mM rATP, and 100 ug/ml BSA) and T4 DNA ligase and was incubated overnight at 14°C. The ligated DNA was then transformed into E. coli FM5 cells by electroporation using a Bio Rad Gene Pulsar apparatus (BioRad, Richmond, CA). A clone was isolated and the plasmid construct verified to contain the two mutations by DNA sequencing. This 'intermediate' vector also contained a deletion of a 193 base pair BsmI to BsmI DNA fragment. The final plasmid vector was constructed by ligation and transformation (as described above) of DNA fragments obtained by cutting and isolating a 2 kilo-base pair SstI to BamHI DNA fragment from the intermediate vector, a 2.8 kbp SstI to EcoRI DNA fragment from the plasmid vector, and a 360 bp BamHI to EcoRI DNA fragment from the plasmid vector. The final construct was verified by DNA sequencing the G-CSF gene. Cultures were grown, and the cells were harvested, and the G-CSF analogs were purified as set forth below.

As indicated above, any combination of mutagenesis techniques may be used to generate a G-CSF analog nucleic acid (and expression product) having one or more than one alteration. The two examples above, using M13-based mutagenesis and gene amplification-based mutagenesis, are illustrative.

E. Expression of G-CSF Analog DNA

The G-CSF analog DNAs were then placed into a plasmid vector and used to transform E. coli strain FM5 (ATCC#53911). The present G-CSF analog DNAs contained on plasmids and in bacterial host cells are available

from the American Type Culture Collection, Rockville, MD, and the accession designations are indicated below.

One liter cultures were grown in broth containing 10g tryptone, 5g yeast extract and 5g NaCl) at 30°C until reaching a density at A^{600} of 0.5, at which point they were rapidly heated to 42°C. The flasks were allowed to continue shaking at for three hours.

Other prokaryotic or eukaryotic host cells may also be used, such as other bacterial cells, strains or species, mammalian cells in culture (COS, CHO or other types) insect cells or multicellular organs or organisms, or plant cells or multicellular organs or organisms, and a skilled practitioner will recognize the appropriate host. The present G-CSF analogs and related compositions may also be prepared synthetically, as, for example, by solid phase peptide synthesis methds, or other chemical manufacturing techniques. Other cloning and expression systems will be apparent to those skilled in the art.

F. Purification of G-CSF Analog Protein

Cells were harvested by centrifugation (10,000 x G, 20 minutes, 4°C). The pellet (usually 5 grams) was resuspended in 30 ml of 1mM DTT and passed three times through a French press cell at 10,000 psi. The broken cell suspension was centrifuged at 10,000g for 30 minutes, the supernatant removed, and the pellet resuspended in 30-40 ml water. This was recentrifuged at 10,000 x G for 30 minutes, and this pellet was dissolved in 25 ml of 2% Sarkosyl and 50mM Tris at pH 8. Copper sulfate was added to a concentration of 40uM, and the mixture was allowed to stir for at least 15 hours at 15-25°C. The mixture was then centrifuged at 20,000 x G for 30 minutes. The resultant solubilized protein mixture was diluted four-fold with 13.3 mM Tris, pH 7.7, the Sarkosyl was removed, and the supernatant was then applied to a DEAE-cellulose (Whatman DE-52) column

equilibrated in 20mM Tris, pH 7.7. After loading and washing the column with the same buffer, the analogs were eluted with 20mM Tris /NaCl (between 35mM to 100mM depending on the analog, as indicated below), pH 7.7. For most of the analogs, the eluent from the DEAE column was adjusted to a pH of 5.4, with 50% acetic acid and diluted as necessary (to obtain the proper conductivity) with 5mM sodium acetate pH 5.4. The solution was then loaded onto a CM-sepharose column equilibrated in 20 mM sodium acetate, pH 5.4. The column was then washed with 20mM NaAc, pH 5.4 until the absorbance at 280 nm was approximately zero. The G-CSF analog was then eluted with sodium acetate/NaCl in concentrations as described below in Table 4. The DEAE column eluents for those analogs not applied to the CM-sepharose column were dialyzed directly into 10mM NaAc, ph 4.0 buffer. The purified G-CSF analogs were then suitably isolated for in vitro analysis. The salt concentrations used for eluting the analogs varied, as noted above. Below, the salt concentrations for the DEAE cellulose column and for the CM-sepharose column are listed:

Table 4

Salt Concentrations

Analog	DEAE Cellulose	CM-Sepharose
Lys^{17}->Arg^{17}	35mM	37.5mM
Lys^{24}->Arg^{24}	35mM	37.5mM
Lys^{35}->Arg^{35}	35mM	37.5mM
Lys^{41}->Arg^{41}	35mM	37.5mM
$Lys^{17,24,35}$->$Arg^{17,24,35}$	35mM	37.5mM
$Lys^{17,35,41}$->$Arg^{17,35,41}$	35mM	37.5mM

Table 4 Con't

Analog	DEAE Cellulose	CM-Sepharose
$Lys^{24,35,41}$->$Arg^{24,35,41}$	35mM	37.5mM
$Lys^{17,24,35,41}$->$Arg^{17,24,35,41}$	35mM	37.5mM
$Lys^{17,24,41}$->$Arg^{17,24,41}$	35mM	37.5mM
Gln^{68}->Glu^{68}	60mM	37,5mM
$Cys^{37,43}$->$Ser^{37,43}$	40mM	37.5mM
Gln^{26}->Ala^{26}	40mM	40mM
Gln^{174}->Ala^{174}	40mM	40mM
Arg^{170}->Ala^{170}	40mM	40mM
Arg^{167}->Ala^{167}	40mM	40mM
Deletion 167*	N/A	N/A
Lys^{41}->Ala^{41}	160mM	40mM
His^{44}->Lys^{44}	40mM	60mM
Glu^{47}->Ala^{47}	40mM	40mM
Arg^{23}->Ala^{23}	40mM	40mM
Lys^{24}->Ala^{24}	120mM	40mM
Glu^{20}->Ala^{20}	40mM	60mM
Asp^{28}->Ala^{28}	40mM	80mM
Met^{127}->Glu^{127}	80mM	40mM
Met^{138}->Glu^{138}	80mM	40mM
Met^{127}->Leu^{127}	40mM	40mM
Met^{138}->Leu^{138}	40mM	40mM
Cys^{18}->Ala^{18}	40mM	37.5mM
$Gln^{12,21}$->$Glu^{12,21}$	60mM	37.5mM
$Gln^{12,21,68}$->$Glu^{12,21,68}$ Glu^{20}->Ala^{20}; Ser^{13}->Gly^{13}	60mM 40mM	37.5mM 80mM

Table 4 Con't

Analog	DEAE Cellulose	CM-Sepharose
$Met^{127,138}$->$Leu^{127,138}$	40mM	40mM
Ser^{13}->Ala^{13}	40mM	40mM
Lys^{17}->Ala^{17}	80mM	40mM
Gln^{121}->Ala^{121}	40mM	60mM
Gln^{21}->Ala^{21}	50mM	Gradient 0 -150mM
His^{44}->Ala^{44}**	40mM	N/A
His^{53}->Ala^{53}**	50mM	N/A
Asp^{110}->Ala^{110}**	40mM	N/A
Asp^{113}->Ala^{113}**	40mM	N/A
Thr^{117}->Ala^{117}**	50mM	N/A
Asp^{28}->Ala^{28}; Asp^{110} Ala^{110}**	50mM	N/A
Glu^{124}->Ala^{124}**	40mM	40mM

* For Deletion ^{167}, the data are unavailable.
** For these analogs, the DEAE cellulose column alone was use for purification.

The above purification methods are illustrative, and a skilled practitioner will recognize that other means are available for obtaining the present G-CSF analogs.

G. Biological Assays

Regardless of which methods were used to create the present G-CSF analogs, the analogs were subject to assays for biological activity. Tritiated thymidine assays were conducted to ascertain the degree of cell division. Other biological assays, however, may be used to ascertain the desired activity. Biological assays such as assaying for the ability to induce terminal differentiation in mouse WEHI-3B (D+) leukemic cell line, also provides indication of G-CSF activity.

See Nicola, et al., Blood 54: 614-27 (1979). Other in vitro assays may be used to ascertain biological activity. See Nicola, Annu. Rev. Biochem. 58: 45-77 (1989). In general, the test for biological activity should provide analysis for the desired result, such as increase or decrease in biological activity (as compared to non-altered G-CSF), different biological activity (as compared to non-altered G-CSF), receptor affinity analysis, or serum half-life analysis. The list is incomplete, and those skilled in the art will recognize other assays useful for testing for the desired end result.

The ^{3}H-thymidine assay was performed using standard methods. Bone marrow was obtained from sacrificed female Balb C mice. Bone marrow cells were briefly suspended, centrifuged, and resuspended in a growth medium. A 160 ul aliquot containing approximately 10,000 cells was placed into each well of a 96 well micro-titer plate. Samples of the purified G-CSF analog(as prepared above) were added to each well, and incubated for 68 hours. Tritiated thymidine was added to the wells and allowed to incubate for 5 additional hours. After the 5 hour incubation time, the cells were harvested, filtered, and thoroughly rinsed. The filters were added to a vial containing scintillation fluid. The beta emissions were counted (LKB Betaplate scintillation counter). Standards and analogs were analyzed in triplicate, and samples which fell substantially above or below the standard curve were re-assayed with the proper dilution. The results reported here are the average of the triplicate analog data relative to the unaltered recombinant human G-CSF standard results.

H. HPLC Analysis

High pressure liquid chromatography was performed on purified samples of analog. Although peak

position on a reverse phase HPLC column is not a definitive indication of structural similarity between two proteins, analogs which have similar retention times may have the same type of hydrophobic interactions with the HPLC column as the non-altered molecule. This is one indication of an overall similar structure.

Samples of the analog and the non-altered recombinant human G-CSF were analyzed on a reverse phase (0.46 x 25 cm) Vydac 214TP54 column (Separations Group, Inc. Hesperia, CA). The purified analog G-CSF samples were prepared in 20 mM acetate and 40 mM NaCl solution buffered at pH 5.2 to a final concentration of 0.1 mg/ml to 5 mg/ml, depending on how the analog performed in the column. Varying amounts (depending on the concentration) were loaded onto the HPLC column, which had been equilibrated with an aqueous solution containing 1% isopropanol, 52.8% acetonitrile, and .38% trifluoro acetate (TFA). The samples were subjected to a gradient of 0.86%/minute acetonitrile, and .002% TFA.

I. Results

Presented below are the results of the above biological assays and HPLC analysis. Biological activity is the average of triplicate data and reported as a percentage of the control standard (non-altered G-CSF). Relative HPLC peak position is the position of the analog G-CSF relative to the control standard (non-altered G-CSF) peak. The "+" or "-" symbols indicate whether the analog HPLC peak was in advance of or followed the control standard peak (in minutes). Not all of the variants had been analyzed for relative HPLC peak, and only those so analyzed are included below. Also presented are the American Type Culture Collection designations for E. coli host cells containing the nucleic acids coding for the present analogs, as prepared above.

Table 5

Seq. ID	Variant	Analog	Relative HPLC Peak	ATCC No.	% Normal G-CSF Activity
67	1	Lys^{17}->Arg^{17}	N/A	69184	N/A
68	2	Lys^{24}->Arg^{24}	N/A	69185	N/A
69	3	Lys^{35}->Arg^{35}	N/A	69186	N/A
70	4	Lys^{41}->Arg^{41}	N/A	69187	N/A
71	5	$Lys^{17,24,35}$->$Arg^{17,24,35}$	N/A	69189	N/A
72	6	$Lys^{17,35,41}$->$Arg^{17,35,41}$	N/A	69192	N/A
73	7	$Lys^{24,35,41}$->$Arg^{24,35,41}$	N/A	69191	N/A
74	8	$Lys^{17,24,35,41}$ ->$Arg^{17,24,35,41}$	N/A	69193	N/A
75	9	$Lys^{17,24,41}$->$Arg^{17,24,41}$	N/A	69190	N/A
76	10	Gln^{68}->Glu^{68}	N/A	69196	N/A
77	11	$Cys^{37,43}$->$Ser^{37,43}$	N/A	69197	N/A
78	12	Gln^{26}->Ala^{26}	+.96	69201	51%
79	13	Gln^{174}->Ala^{174}	+.14	69202	100%
80	14	Arg^{170}->Ala^{170}	+.78	69203	100%

Table 5 Con't

Seq. ID	Variant	Analog	Relative HPLC Peak	ATCC No.	% Normal G-CSF Activity
81	15	Arg^{167}->Ala^{167}	+.54	69204	110%
82	16	Deletion 167	-.99	69207	N/A
83	17	Lys^{41}->Ala^{41}	+.25	69208	81%
84	18	His^{44}->Lys^{44}	-1.53	69212	70%
85	19	Glu^{47}->Ala^{47}	+.14	69205	0%
86	20	Arg^{23}->Ala^{23}	-.03	69206	31%
87	21	Lys^{24}->Ala^{24}	+1.95	69213	0%
88	22	Glu^{20}->Ala^{20}	-0.07	69211	0%
89	23	Asp^{28}->Ala^{28}	-.30	69210	147%
90	24	Met^{127}->Glu^{127}	N/A	69223	N/A
91	25	Met^{138}->Glu^{138}	N/A	69222	N/A
92	26	Met^{127}->Leu^{127}	N/A	69198	N/A
93	27	Met^{138}->Leu^{138}	N/A	69199	N/A
94	28	Cys^{18}->Ala^{18}	N/A	69188	N/A
95	29	$Gln^{12,21}$->$Glu^{12,21}$	N/A	69194	N/A
96	30	$Gln^{12,21,68}$->$Glu^{12,21,68}$	N/A	69195	N/A
97	31	Glu^{20}->Ala^{20}; Ser^{13}	+1.74	69209	0%

Table 5 Con't

Seq. ID	Variant	Analog	Relative HPLC Peak	ATCC No.	% Normal G-CSF Activity
		->Gly^{13}			
98	32	$Met^{127,138}$->$Leu^{127,138}$	+1.43	69200	98%
99	33	Ser^{13}->Ala^{13}	0	69221	110%
100	34	Lys^{17}->Ala^{17}	+.50	69226	70%
101	35	Gln^{121}->Ala^{121}	+2.7	69225	100%
102	36	Gln^{21}->Ala^{21}	+0.63	69217	9.6%
103	37	His^{44}->Ala^{44}	+1.52	69215	10.8%
104	38	His^{53}->Ala^{53}	+0.99	69219	8.3%
105	39	Asp^{110}->Ala^{110}	+1.97	69216	29%
106	40	Asp^{113}->Ala^{113}	-0.34	69218	0%
107	41	Thr^{117}->Ala^{117}	+0.4	69214	9.7%
108	42	Asp^{28}->Ala^{28}; Asp^{110} Ala^{110}	+3.2	69220	20.6%

Table 5 Con't

Seq. ID	Variant	Analog	Relative HPLC Peak	ATCC No.	% Normal G-CSF Activity
109	43	Glu^{124}->Ala^{124}	+0.16	69224	75%
110	44	Phe^{114}->Val^{114}, T^{117}->A^{117}**	+0.53		0%

**This analog was apparently a result of an inadvertent error in the oligo which was used to prepare number 41, above (Thr^{117}->Ala^{117}), and thus was prepared identically to the process used for that analog.

"N/A" indicates data which are not available.

1. Identification of Structure-Function Relationships

The first step used to design the present analogs was to determine what moieties are necessary for structural integrity of the G-CSF molecule. This was done at the amino acid residue level, although the atomic level is also available for analysis. Modification of the residues necessary for structural integrity results in change in the overall structure of the G-CSF molecule. This may or may not be desirable, depending on the analog one wishes to produce. The working examples here were designed to maintain the overall structural integrity of the G-CSF molecule, for the purpose of maintain G-CSF receptor binding of the analog to the G-CSF receptor (as used in this section below, the "G-CSF receptor" refers to the natural G-CSF receptor, found on hematopoietic cells). It was assumed, and confirmed by the studies presented here, that G-CSF receptor binding is a necessary step for at least one biological activity, as determined by the above biological assays.

As can be seen from the figures, G-CSF (here, recombinant human met-G-CSF) is an antiparallel 4-alpha helical bundle with a left-handed twist, and with overall dimensions of 45 Å x 30Å x 24Å. The four helices within the bundle are referred to as helices A, B, C and D, and their connecting loops are known as the AB, BC and CD loops. The helix crossing angles range from -167.5° to -159.4°. Helices A, B, and C are straight, whereas helix D contains two kinds of structural characteristics, at Gly 150 and Ser 160 (of the recombinant human met-G-CSF). Overall, the G-CSF molecules is a bundle of four helices, connected in series by external loops. This structural information was then correlated with known functional information. It was known that residues (including methionine at

position 1) 47, 23, 24, 20, 21, 44, 53, 113, 110, 28 and 114 may be modified, and the effect on biological activity would be substantial.

The majority of single mutations which lowered biological activity were centered around two regions of G-CSF that are separated by 30Å, and are located on different faces of the four helix bundle. One region involves interactions between the A helix and the D helix. This is further confirmed by the presence of salt bridges in the non-altered molecule as follows:

Atom	Helix	Atom	Helix	Distance
Arg 170 N1	D	Tyr 166 OH	A	3.3
Tyr 166 OH	D	Arg 23 N2	A	3.3
Glu 163 OE1	D	Arg 23 N1	A	2.8
Arg 23 N1	A	Gln 26 OE1	A	3.1
Gln 159 NE2	D	Gln 26 O	A	3.3

Distances reported here were for molecule A, as indicated in FIGURE 5 (wherein three G-CSF molecules crystallized together and were designated as A, B, and C). As can be seen, there is a web of salt bridges between helix A and helix D, which act to stabilize the helix A structure, and therefore affect the overall structure of the G-CSF molecule.

The area centering around residues Glu 20, Arg 23 and Lys 24 are found on the hydrophilic face of the A helix (residues 20-37). Substitution of the residues with the non-charged alanine residue at positions 20 and 23 resulted in similar HPLC retention times, indicating similarity in structure. Alteration of these sites altered the biological activity (as indicated by the present assays). Substitution at Lys 24 altered biological activity, but did not result in a similar HPLC retention time as the other two alterations.

The second site at which alteration lowered biological activity involves the AB helix. Changing glutamine at position 47 to alanine (analog no. 19, above) reduced biological activity (in the thymidine uptake assay) to zero. The AB helix is predominantly hydrophobic, except at the amino and carboxy termini; it contains one turn of a 3^{10} helix. There are two histadines at each termini (His 44 and His 56) and an additional glutamate at residue 46 which has the potential to form a salt bridge to His 44. The fourier transformed infra red spectrographic analysis (FTIR) of the analog suggests this analog is structurally similar to the non-altered recombinant G-CSF molecule. Further testing showed that this analog would not crystallize under the same conditions as the non-altered recombinant molecule.

Alterations at the carboxy terminus (Gln 174, Arg 167 and Arg 170) had little effect on biological activity. In contrast, deletion of the last eight residues (167-175) lowered biological activity. These results may indicate that the deletion destabilizes the overall structure which prevents the mutant from proper binding to the G-CSF receptor (and thus initiating signal transduction).

Generally, for the G-CSF internal core -- the internal four helix bundle lacking the external loops -- the hydrophobic internal residues are essential for structural integrity. For example, in helix A, the internal hydrophobic residues are (with methionine being position 1) Phe 14, Cys 18, Val 22, Ile 25, Ile 32 and Leu 36. Generally, for the G-CSF internal core -- the internal four helix bundle lacking the external loops -- the hydrophobic internal residues are essential for structural integrity. For example, in helix A, the internal hydrophobic residues are (with methionine being position 1 as in FIGURE 1) Phe 14, Cys 18, Val 22, Ile

25, Ile 32 and Leu 36. The other hydrophobic residues (again with the met at position 1) are: helix B, Ala 72, Leu 76, Leu 79, Leu 83, Tyr 86, Leu 90 Leu 93; helix C, Leu 104, Leu 107, Val 111, Ala 114, Ile 118, Met 122; and helix D, Val 154, Val 158, Phe 161, Val 164, Val 168, Leu 172.

The above biological activity data, from the presently prepared G-CSF analogs, demonstrate that modification of the external loops interfere least with G-CSF overall structure. Preferred loops for analog prepration are the AB loop and the CD loop. The loops are relatively flexible structures as compared to the helices. The loops may contribute to the proteolysis of the molecule. G-CSF is relatively fast acting in vivo as the purpose the molecule serves is to generate a response to a biological challenge, i.e., selectively stimulate neutrophils. The G-CSF turnover rate is also relatively fast. The flexibility of the loops may provide a "handle" for proteases to attach to the molecule to inactivate the molecule. Modification of the loops to prevent protease degradation, yet have (via retention of the overall structure of non-modified G-CSF) no loss in biological activity may be accomplished.

This phenomenon is probably not limited to the G-CSF molecule but may also be common to the other molecules with known similar overall structures, as presented in Figure 2. Alteration of the external loop of, for example hGH, Interferon B, IL-2, GM-CSF and IL-4 may provide the least change to the overall structure. The external loops on the GM-CSF molecule are not as flexible as those found on the G-CSF molecule, and this may indicate a longer serum life, consistent with the broader biological activity of GM-CSF. Thus, the external loops of GM-CSF may be modified by releasing the external loops from the beta-sheet structure, which

may make the loops more flexible (similar to those G-CSF) and therefore make the molecule more susceptible to protease degradation (and thus increase the turnover rate).

Alteration of these external loops may be effected by stabilizing the loops by connection to one or more of the internal helices. Connecting means are known to those in the art, such as the formation of a beta sheet, salt bridge, disulfide bonding or hydrophobic interactions, and other means are available. Also, deletion of one or more moieties, such as one or more amino acid residues or portions thereof, to prepare an abbreviated molecule and thus eliminate certain portions of the external loops may be effected.

Thus, by alteration of the external loops, preferably the AB loop (amino acids 58-72 of r-hu-met G-CSF) or the CD loop (amino acids 119 to 145 of r-hu-met-G-CSF), and less preferably the amino terminus (amino acids 1-10), one may therefore modify the biological function without elimination of G-CSF G-CSF receptor binding. For example, one may: (1) increase half-life (or prepare an oral dosage form, for example) of the G-CSF molecule by, for example, decreasing the ability of proteases to act on the G-CSF molecule or adding chemical modifications to the G-CSF molecule, such as one or more polyethylene glycol molecules or enteric coatings for oral formulation which would act to change some characteristic of the G-CSF molecule as described above, such as increasing serum or other half-life or decreasing antigenicity; (2) prepare a hybrid molecule, such as combining G-CSF with part or all of another protein such as another cytokine or another protein which effects signal transduction via entry through the cell through a G-CSF G-CSF receptor transport mechanism; or (3) increase the biological activity as in, for example, the ability to selectively

stimulate neutrophils (as compared to a non-modified G-CSF molecule). This list is not limited to the above exemplars.

Another aspect observed from the above data is that stabilizing surface interactions may affect biological activity. This is apparent from comparing analogs 23 and 40. Analog 23 contains a substitution of the charged asparagine residue at position 28 for the neutrally-charged alanine residue in that position, and such substitution resulted in a 50% increase in the biological activity (as measured by the disclosed thymidine uptake assays). The asparagine residue at position 28 has a surface interaction with the asparagine residue at position 113; both residues being negatively charged, there is a certain amount of instability (due to the repelling of like charged moieties). When, however the asparagine at position 113 is replaced with the neutrally-charged alanine, the biological activity drops to zero (in the present assay system). This indicates that the asparagine at position 113 is critical to biological activity, and elimination of the asparagine at position 28 serves to increase the effect that asparagine at position 113 possesses.

The domains required for G-CSF receptor binding were also determined based on the above analogs prepared and the G-CSF structure. The G-CSF receptor binding domain is located at residues (with methionine being position 1) 11-57 (between the A and AB helix) and 100-118 (between the B and C helices). One may also prepare abbreviated molecules capable of binding to a G-CSF receptor and initiate signal transduction for selectively stimulating neutrophils by changing the external loop structure and having the receptor binding domains remain intact.

Residues essential for biological activity and presumably G-CSF receptor binding or signal transduction

have been identified. Two distinct sites are located on two different regions of the secondary structure. What is here called "Site A" is located on a helix which is constrained by salt bridge contacts between two other members of the helical bundle. The second site, "Site B" is located on a relatively more flexible helix, AB. The AB helix is potentially more sensitive to local pH changes because of the type and position of the residues at the carboxy and amino termini. The functional importance of this flexible helix may be important in a conformationally induced fit when binding to the G-CSF receptor. Additionally, the extended portion of the D helix is also indicated to be a G-CSF receptor binding domain, as ascertained by direct mutational and indirect comparative protein structure analysis. Deletion of the carboxy terminal end of r-hu-met-G-CSF reduces activity as it does for hGH, see, Cunningham and Wells, Science 244: 1081-1084 (1989). Cytokines which have similar structures, such as IL-6 and GM-CSF with predicted similar topology also center their biological activity along the carboxy end of the D helix, see Bazan, Immunology Today 11: 350-354 (1990)

A comparison of the structures and the positions of G-CSF receptor binding determinants between G-CSF and hGH suggests both molecules have similar means of signal transduction. Two separate G-CSF receptor binding sites have been identified for hGH De Vos et al., Science 255: 306-32 (1991). One of these binding sites (called "Site I") is formed by residues on the exposed faces of hGH's helix 1, the connection region between helix 1 and 2, and helix 4. The second binding site (called "Site II") is formed by surface residues of helix 1 and helix 3.

The G-CSF receptor binding determinates identified for G-CSF are located in the same relative positions as those identified for hGH. The G-CSF

receptor binding site located in the connecting region between helix A and B on the AB helix (Site A) is similar in position to that reported for a small piece of helix (residues 38-47) of hGH. A single point mutation in the AB helix of G-CSF significantly reduces biological activity (as ascertained in the present assays), indicating the role in a G-CSF receptor-ligand interface. Binding of the G-CSF receptor may destabilize the 3^{10} helical nature of this region and induce a conformation change improving the binding energy of the ligand/G-CSF receptor complex.

In the hGH receptor complex, the first helix of the bundle donates residues to both of the binding sites required to dimerize the hGH receptor Mutational analysis of the corresponding helix of G-CSF (helix A) has identified three residues which are required for biological activity. Of these three residues, Glu 20 and Arg 24 lie on one face of the helical bundle towards helix C, whereas the side chain of Arg 23 (in two of the three molecules in the asymmetric unit) points to the face of the bundle towards helix D. The position of side chains of these biologically important residues indicates that similar to hGH, G-CSF may have a second G-CSF receptor binding site along the interface between helix A and helix C. In contrast with the hGH molecule, the amino terminus of G-CSF has a limited biological role as deletion of the first 11 residues has little effect on the biological activity.

As indicated above (see FIGURE 2, for example), G-CSF has a topological similarity with other cytokines. A correlation of the structure with previous biochemical studies, mutational analysis and direct comparison of specific residues of the hGH receptor complex indicates that G-CSF has two receptor binding sites. Site A lies along the interface of the A and D helices and includes residues in the small AB helix.

Site B also includes residues in the A helix but lies along the interface between helices A and C. The conservation of structure and relative positions of biologically important residues between G-CSF and hGH is one indication of a common method of signal transduction in that the receptor is bound in two places. It is therefore found that G-CSF analogs possessing altered G-CSF receptor binding domains may be prepared by alteration at either of the G-CSF receptor binding sites (residues 20-57 and 145-175).

Knowledge of the three dimensional structure and correlation of the composition of G-CSF protein makes possible a systematic, rational method for preparing G-CSF analogs. The above working examples have demonstrated that the limitations of the size and polarity of the side chains within the core of the structure dictate how much change the molecule can tolerate before the overall structure is changed.

SEQUENCE LISTING

(1) GENERAL INFORMATION:

(i) APPLICANT: Amgen Inc.

(ii) TITLE OF INVENTION: G-CSF ANALOG COMPOSITIONS AND METHODS

(iii) NUMBER OF SEQUENCES: 110

(iv) CORRESPONDENCE ADDRESS:
(A) ADDRESSEE: Amgen, Inc.
(B) STREET: Amgen Center, 1840 DeHavilland Drive
(C) CITY: Thousand Oaks
(D) STATE: California
(E) COUNTRY: United States of America
(F) ZIP: 91320-1789

(v) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.25

(vi) CURRENT APPLICATION DATA:
(A) APPLICATION NUMBER:
(B) FILING DATE:
(C) CLASSIFICATION:

(viii) ATTORNEY/AGENT INFORMATION:
(A) NAME: Pessin, Karol
(B) REGISTRATION NUMBER: 34,899

(ix) TELECOMMUNICATION INFORMATION:
(A) TELEPHONE: 805/499-5725
(B) TELEFAX: 805/499-8011

(2) INFORMATION FOR SEQ ID NO:1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 565 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA (genomic)

(ix) FEATURE:
(A) NAME/KEY: CDS
(B) LOCATION: 30..554

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:1:

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TCTAGAAAAA ACCAAGGAGG TAATAAATA ATG ACT CCA TTA GGT CCT GCT TCT        53
                                    Met Thr Pro Leu Gly Pro Ala Ser
                                      1               5

TCT CTG CCG CAA AGC TTT CTG CTG AAA TGT CTG GAA CAG GTT CGT AAA       101
Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln Val Arg Lys
      10                  15                  20

ATC CAG GGT GAC GGT GCT GCA CTG CAA GAA AAA CTG TGC GCT ACT TAC       149
Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu Cys Ala Thr Tyr
 25                  30                  35                  40

AAA CTG TGC CAT CCG GAA GAA CTG GTA CTG CTG GGT CAT TCT CTT GGG       197
Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu Gly His Ser Leu Gly
                    45                  50                  55

ATC CCG TGG GCT CCG CTG TCT TCT TGC CCA TCT CAA GCT CTT CAG CTG       245
Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro Ser Gln Ala Leu Gln Leu
               60                  65                  70

GCT GGT TGT CTG TCT CAA CTG CAT TCT GGT CTG TTC CTG TAT CAG GGT       293
Ala Gly Cys Leu Ser Gln Leu His Ser Gly Leu Phe Leu Tyr Gln Gly
          75                  80                  85

CTT CTG CAA GCT CTG GAA GGT ATC TCT CCG GAA CTG GGT CCG ACT CTG       341
Leu Leu Gln Ala Leu Glu Gly Ile Ser Pro Glu Leu Gly Pro Thr Leu
      90                  95                  100

GAC ACT CTG CAG CTA GAT GTA GCT GAC TTT GCT ACT ACT ATT TGG CAA       389
Asp Thr Leu Gln Leu Asp Val Ala Asp Phe Ala Thr Thr Ile Trp Gln
105                 110                 115                 120

CAG ATG GAA GAG CTC GGT ATG GCA CCA GCT CTG CAA CCG ACT CAA GGT       437
Gln Met Glu Glu Leu Gly Met Ala Pro Ala Leu Gln Pro Thr Gln Gly
                  125                 130                 135

GCT ATG CCG GCA TTC GCT TCT GCA TTC CAG CGT CGT GCA GGA GGT GTA       485
Ala Met Pro Ala Phe Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val
              140                 145                 150

CTG GTT GCT TCT CAT CTG CAA TCT TTC CTG GAA GTA TCT TAC CGT GTT       533
Leu Val Ala Ser His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val
         155                 160                 165

CTG CGT CAT CTG GCT CAG CCG TAATAGAATT C                              565
Leu Arg His Leu Ala Gln Pro
     170                 175
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(2) INFORMATION FOR SEQ ID NO:2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:2:

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Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
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(2) INFORMATION FOR SEQ ID NO:3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:3:

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CTTTCTGCTG CGTTGTCTGG AACA                                          24
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(2) INFORMATION FOR SEQ ID NO:4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:4:

ACAGGTTCGT CGTATCCAGG GTG 23

(2) INFORMATION FOR SEQ ID NO:5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:5:

CACTGCAAGA ACGTCTGTGC GTC 23

(2) INFORMATION FOR SEQ ID NO:6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:6:

CGCTACTTAC CGTCTGTGCC ATC 23

(2) INFORMATION FOR SEQ ID NO:7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:7:

CTTTCTGCTG CGTTGTCTGG AACA 24

(2) INFORMATION FOR SEQ ID NO:8:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:8:

ACAGGTTCGT CGTATCCAGG GTG 23

(2) INFORMATION FOR SEQ ID NO:9:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:9:

CACTGCAAGA ACGTCTGTGC GCT 23

(2) INFORMATION FOR SEQ ID NO:10:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:10:

CTTTCTGCTG CGTTGTCTGG AACA 24

(2) INFORMATION FOR SEQ ID NO:11:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:11:

ACAGGTTCGT CGTATCCAGG GTG 23

(2) INFORMATION FOR SEQ ID NO:12:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:12:

CGCTACTTAC CGTCTGTCCC ATC 23

(2) INFORMATION FOR SEQ ID NO:13:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:13:

CTTTCTGCTG CGTTGTCTGG AACA 24

(2) INFORMATION FOR SEQ ID NO:14:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:14:

CACTGCAAGA ACGTCTGTGC GCT 23

(2) INFORMATION FOR SEQ ID NO:15:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:15:

CGCTACTTAC CGTCTGTGCC ATC 23

(2) INFORMATION FOR SEQ ID NO:16:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:16:

ACAGGTTCGT CGTATCCAGG GTG 23

(2) INFORMATION FOR SEQ ID NO:17:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:17:

CACTGCAAGA ACGTCTGTGC GCT 23

(2) INFORMATION FOR SEQ ID NO:18:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:18:

CGCTACTTAC CGTCTGTGCC ATC 23

(2) INFORMATION FOR SEQ ID NO:19:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:19:

CTTTCTGCTG CGTTGTCTGG AACA 24

(2) INFORMATION FOR SEQ ID NO:20:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:20:

ACAGGTTCGT CGTATCCAGG GTG 23

(2) INFORMATION FOR SEQ ID NO:21:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:21:

CACTGCAAGA ACGTCTGTGC GCT 23

(2) INFORMATION FOR SEQ ID NO:22:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:22:

CGCTACTTAC CGTCTGTGCC ATC 23

(2) INFORMATION FOR SEQ ID NO:23:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:23:

TCTGCTGAAA GCTCTGGAAC AGG 23

(2) INFORMATION FOR SEQ ID NO:24:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:24:

CTTGTCCATC TGAAGCTCTT CAG 23

(2) INFORMATION FOR SEQ ID NO:25:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 37 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:25:

GAAAAACTGT CCGCTACTTA CAAACTGTCC CATCCGG 37

(2) INFORMATION FOR SEQ ID NO:26:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:26:

TTCGTAAAAT CGCGGGTGAC GG 22

(2) INFORMATION FOR SEQ ID NO:27:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:27:

TCATCTGGCT GCGCCGTAAT AG 22

(2) INFORMATION FOR SEQ ID NO:28:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:28:

CCGTGTTCTG GCTCATCTGG CT 22

(2) INFORMATION FOR SEQ ID NO:29:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:29:

GAAGTATCTT ACGCTGTTCT GCGT 24

(2) INFORMATION FOR SEQ ID NO:30:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:30:

GAAGTATCTT ACTAAGTTCT GCGTC 25

(2) INFORMATION FOR SEQ ID NO:31:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:31:

CGCTACTTAC GCACTGTGCC AT 22

(2) INFORMATION FOR SEQ ID NO:32:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:32:

CAAACTGTGC AAGCCGGAAG AG 22

(2) INFORMATION FOR SEQ ID NO:33:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:33:

CATCCGGAAG CACTGGTACT GC 22

(2) INFORMATION FOR SEQ ID NO:34:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:34:

GGAACAGGTT GCTAAAATCC AGG 23

(2) INFORMATION FOR SEQ ID NO:35:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:35:

GAACAGGTTC GTGCGATCCA GGGTG 25

(2) INFORMATION FOR SEQ ID NO:36:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:36:

GAAATGTCTG GCACAGGTTC GT 22

(2) INFORMATION FOR SEQ ID NO:37:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:37:

TCCAGGGTGC CGGTGCTGC 19

(2) INFORMATION FOR SEQ ID NO:38:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:38:

AAGAGCTCGG TGAGGCACCA GCT 23

(2) INFORMATION FOR SEQ ID NO:39:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:39:

CTCAAGGTGC TGAGCCGGCA TTC 23

(2) INFORMATION FOR SEQ ID NO:40:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:40:

GAGCTCGGTC TGGCACCAGC 20

(2) INFORMATION FOR SEQ ID NO:41:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:41:

TCAAGGTGCT CTGCCGGCAT T 21

(2) INFORMATION FOR SEQ ID NO:42:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:42:

TCTGCCGCAA GCCTTTCTGC TGA 23

(2) INFORMATION FOR SEQ ID NO:43:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:43:

CTTTCTGCTG GCATGTCTGG AACA 24

(2) INFORMATION FOR SEQ ID NO:44:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:44:

CTATTTGGCA AGCGATGGAA GAGC 24

(2) INFORMATION FOR SEQ ID NO:45:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:45:

CAGATGGAAG CGCTCGGTAT G 21

(2) INFORMATION FOR SEQ ID NO:46:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:46:

GAGCTCGGTC TGGCACCAGC 20

(2) INFORMATION FOR SEQ ID NO:47:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:47:

TCAAGGTGCT CTGCCGGCAT T 21

(2) INFORMATION FOR SEQ ID NO:48:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:48:

GAAATGTCTG GCACAGGTTC GT 22

(2) INFORMATION FOR SEQ ID NO:49:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:49:

TTCCGGAGCG CACAGTTTG 19

(2) INFORMATION FOR SEQ ID NO:50:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:50:

CGAGAAGGCC TCGGGTGTCA AAC 23

(2) INFORMATION FOR SEQ ID NO:51:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:51:

ATGCCAAATT GCAGTAGCAA AG 22

(2) INFORMATION FOR SEQ ID NO:52:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:52:

ACAACGGTTT AACGTCATCG TTTC 24

(2) INFORMATION FOR SEQ ID NO:53:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:53:

ATCAGCTACT GCTAGCTGCA GA 22

(2) INFORMATION FOR SEQ ID NO:54:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 23 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:54:

TCAGTCGATG ACGATCGACG TCT 23

(2) INFORMATION FOR SEQ ID NO:55:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:55:

TTACGAACCG CTTCCAGACA TT 22

(2) INFORMATION FOR SEQ ID NO:56:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:56:

TAAAATGCTT GGCGAAGGTC TGTAA 25

(2) INFORMATION FOR SEQ ID NO:57:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:57:

GTAGCAAATG CAGCTACATC TA 22

(2) INFORMATION FOR SEQ ID NO:58:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 25 base pairs
(B) TYPE: nucleic acid

(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:58:

CATCATCGTT TACGTCGATG TAGAT 25

(2) INFORMATION FOR SEQ ID NO:59:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:59:

CCAAGAGAAG CACCCAGCAG 20

(2) INFORMATION FOR SEQ ID NO:60:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 22 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:60:

AGGGTTCTCT TCGTGGGTCG TC 22

(2) INFORMATION FOR SEQ ID NO:61:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 20 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:61:

CACTGGCGGT GATAATGAGC 20

(2) INFORMATION FOR SEQ ID NO:62:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 19 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:62:

CTAGGCCAGG CATTACTGG 19

(2) INFORMATION FOR SEQ ID NO:63:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 21 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:63:

CCACTGGCGG TGATACTGAG C 21

(2) INFORMATION FOR SEQ ID NO:64:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:64:

AGCAGAAAGC TTTCCGGCAG AGAAGAAGCA GGA 33

(2) INFORMATION FOR SEQ ID NO:65:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 54 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:65:

GCCGCAAAGC TTTCTGCTGA AATGTCTGGA AGAGGTTCGT AAAATCCAGG GTGA 54

(2) INFORMATION FOR SEQ ID NO:66:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 59 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: DNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:66:

CTGGAATGCA GAAGCAAATG CCGGCATAGC ACCTTCAGTC GGTTGCAGAG CTGGTGCCA 59

(2) INFORMATION FOR SEQ ID NO:67:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:67:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Arg Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:68:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:68:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Arg Ile Gln Gly Asp Gly Ala Ala Leu
                20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
            35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
        50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:69:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:69:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Arg Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:70:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:70:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Arg Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60
```

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:71:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:71:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Arg Cys Leu Glu Gln Val Arg Arg Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Arg Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

```
Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
     130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                    165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:72:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:72:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1               5                  10                  15

Arg Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
                20                  25                  30

Gln Glu Arg Leu Cys Ala Thr Tyr Arg Leu Cys His Pro Glu Glu Leu
            35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
      50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                    85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
               100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
          115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
     130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                    165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:73:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:73:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Arg Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Arg Leu Cys Ala Thr Tyr Arg Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:74:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:74:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Arg Cys Leu Glu Gln Val Arg Arg Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Arg Leu Cys Ala Thr Tyr Arg Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:75:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:75:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Arg Cys Leu Glu Gln Val Arg Arg Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Arg Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:76:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:76:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Glu Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala

115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:77:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:77:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Ser Ala Thr Tyr Lys Leu Ser His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:78:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:78:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Ala Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:79:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:79:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15
```

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Ala Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:80:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:80:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Ala His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:81:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:81:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

```
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Ala Val Leu Arg His Leu Ala Gln Pro
                  165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:82:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 174 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:82:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
             20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
          35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
      50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                  85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
             100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
          115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
      130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Val Leu Arg His Leu Ala Gln Pro
                  165                 170             174
```

(2) INFORMATION FOR SEQ ID NO:83:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:83:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Ala Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:84:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:84:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys Lys Pro Glu Glu Leu
        35                  40                  45
```

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:85:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:85:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Ala Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:86:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:86:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Ala Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:87:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:87:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Ala Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:88:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:88:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Ala Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:89:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:89:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Ala Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60
```

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:90:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein
(xi) SEQUENCE DESCRIPTION: SEQ ID NO:90:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Glu Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

```
Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                    165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:91:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:91:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
                20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
            35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
        50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Glu Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                    165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:92:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:92:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Leu Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:93:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:93:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30
```

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Leu Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:94:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:94:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Ala Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:95:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:95:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Glu Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Glu Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:96:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:96:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Glu Ser Phe Leu Leu
  1               5                  10                  15

Lys Cys Leu Glu Glu Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
             20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
         35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
     50                  55                  60

Cys Pro Ser Glu Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                 85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:97:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:97:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Gly Phe Leu Leu
1 5 10 15

Lys Cys Leu Ala Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:98:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:98:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Leu Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Leu Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:99:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:99:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ala Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

```
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
         115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
     130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                   165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:100:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:100:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1               5                  10                  15

Ala Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
                20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
           35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
       50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                   85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
               100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
         115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
     130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                   165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:101:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:101:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Ala Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:102:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:102:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15
```

Lys Cys Leu Glu Ala Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:103:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:103:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys Ala Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:104:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:104:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly Ala Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:105:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:105:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Ala Val Ala
100 105 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

(2) INFORMATION FOR SEQ ID NO:106:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:106:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
        35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
    50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
            100                 105                 110

Ala Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
        115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
    130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
            165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:107:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:107:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
 1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
            20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
        35                  40                  45
```

```
Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
      50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                    85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
               100                 105                 110

Asp Phe Ala Thr Ala Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
          115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
     130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                   165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:108:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:108:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Ala Gly Ala Ala Leu
               20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
          35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
      50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                    85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Ala Val Ala
               100                 105                 110
```

```
Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
          115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
     130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                    165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:109:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:109:

```
Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
  1               5                  10                  15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
                20                  25                  30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
           35                  40                  45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
      50                  55                  60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
 65                  70                  75                  80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
                    85                  90                  95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
               100                 105                 110

Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Ala Leu Gly Met Ala
          115                 120                 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
     130                 135                 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145                 150                 155                 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
                    165                 170                 175
```

(2) INFORMATION FOR SEQ ID NO:110:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 175 amino acids
(B) TYPE: amino acid
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO:110:

Met Thr Pro Leu Gly Pro Ala Ser Ser Leu Pro Gln Ser Phe Leu Leu
1 5 10 15

Lys Cys Leu Glu Gln Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu
20 25 30

Gln Glu Lys Leu Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu
35 40 45

Val Leu Leu Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser
50 55 60

Cys Pro Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His
65 70 75 80

Ser Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
85 90 95

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val Ala
100 105 110

Asp Val Ala Thr Ala Ile Trp Gln Gln Met Glu Glu Leu Gly Met Ala
115 120 125

Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe Ala Ser Ala
130 135 140

Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser His Leu Gln Ser
145 150 155 160

Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His Leu Ala Gln Pro
165 170 175

WHAT IS CLAIMED IS:

1. A method for preparing a G-CSF analog comprising the steps of:

(a) viewing information conveying the three dimensional structure of a G-CSF molecule;

(b) selecting from said viewed information at least one site on said G-CSF molecule for alteration;

(c) preparing a G-CSF molecule having such alteration; and

(d) optionally, testing such G-CSF molecule for a desired characteristic.

2. A computer based method for preparing a G-CSF analog comprising the steps of:

(a) providing computer expression of the three dimensional structure of a G-CSF molecule;

(b) selecting from said computer expression at least one site on said G-CSF molecule for alteration;

(c) preparing a G-CSF molecule having such alteration; and,

(d) optionally, testing such G-CSF molecule for a desired characteristic.

3. A method for preparing a G-CSF analog with the aid of a computer comprising:

(a) providing said computer with the means for displaying the three dimensional structure of a G-CSF molecule including displaying the composition of moieties of said G-CSF molecule, preferably displaying the three dimensional location of each amino acid, and more preferably displaying the three dimensional location of each atom of a G-CSF molecule;

(b) viewing said display;

(c) selecting a site on said display for alteration in the composition of said molecule or the location of a moiety; and

(d) preparing a G-CSF analog with such alteration.

4. A computer-based method for preparing a G-CSF analog comprising the steps of:

(a) viewing the three dimensional structure of a G-CSF molecule via a computer, said computer having been previously programmed (i) to express the coordinates of a G-CSF molecule in three dimensional space, and (ii) to allow for entry of information for alteration of said G-CSF expression and viewing thereof;

(b) selecting a site on said visual image of said G-CSF molecule for alteration;

(c) entering information for said alteration on said computer;

(d) viewing a three dimensional structure of said altered G-CSF molecule via said computer;

(e) optionally repeating steps (a)-(e) above;

(f) preparing a G-CSF analog with said alteration; and

(g) optionally testing said G-CSF analog for a desired characteristic.

5. In a computer-based apparatus for displaying the three dimensional structure of a molecule, the improvement comprising means for correlating said three dimensional structure of a G-CSF molecule with the composition of said G-CSF molecule.

6. A method for crystallization of a protein comprising the steps of:

(a) combining, optionally by automated means, aqueous aliquots of said protein with either (i) aliquots of a salt solution, each aliquot having a different concentration of salt; or (ii) aliquots of a

precipitant solution, each aliquot having a different concentration of precipitant;

(b) selecting at least one of said combined aliquots, said selection based on the formation of precrystalline forms, or, if no precrystalline forms are so produced, increasing the protein starting concentration of said aqueous aliquots of protein and repeating step (a);

(c) after said salt or said precipitant concentration is selected, repeating step (a) with said previously unselected solution in the presence of said selected concentration; and,

(d) repeating step (b) and step (a) until a crystal of desired quality is obtained.

7. A method of claim 6 wherein each combination pursuant to step (a) is performed in a range of pH.

8. A method of claim 6 wherein said combining of step (a) is done in the presence of a nucleation initiation unit.

9. A G-CSF analog having an amino acid sequence different from that of Figure 1 in that:

(a) the N-terminal methionine is optional; and

(b) one or more of amino acids 58-72 (i) is substituted with one or more different amino acids or (ii) deleted; or (iii) chemically modified.

10. A G-CSF analog of claim 9 wherein said analog is more resistant to proteolysis than a G-CSF molecule of Figure 1.

11. A G-CSF analog of claim 10 wherein at least one of said amino acids is chemically modified by the addition of a polyethylene glycol molecule.

12. A G-CSF analog having an amino acid sequence different from that of Figure 1 in that:

(a) the N-terminal methionine is optional; and

(b) one or more of amino acids 119-125 (i) is substituted with one or more different amino acids or (ii) deleted; or (iii) chemically modified.

13. A G-CSF analog of claim 12 wherein said analog is more resistant to proteolysis than a G-CSF molecule of Figure 1.

14 A G-CSF analog of claim 12 wherein at least one of said amino acids is chemically modified by the addition of a polyethylene glycol molecule.

15. A G-CSF molecule having the AB loop stabilized by connecting such loop to one or more of helices A, B, C, or D.

16. A G-CSF molecule having the CD loop stabilized by connecting such loop to one or more of helices A, B, C, or D.

17. A G-CSF analog, optionally in a pharmaceutically effective carrier, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys^{17}->Arg^{17} and the N-terminal methionine is optional.

18. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys^{35}->Arg^{35} and the N-terminal methionine is optional.

19. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys^{41}->Arg^{41} and the N-terminal methionine is optional.

20. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that

$Lys^{17,24,35}$->$Arg^{17,24,35}$ and the N-terminal methionine is optional.

21. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that $Lys^{17,35,41}$->$Arg^{17,35,41}$ and the N-terminal methionine is optional.

22. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that $Lys^{24,35,41}$->$Arg^{24,35,41}$ and the N-terminal methionine is optional.

23. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that $Lys^{17,24,35,41}$ ->$Arg^{17,24,35,41}$ and the N-terminal methionine is optional.

24. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that $Lys^{17,24,41}$->$Arg^{17,24,41}$ and the N-terminal methionine is optional.

25. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln^{68}->Glu^{68} and the N-terminal methionine is optional.

26. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that $Cys^{37,43}$->$Ser^{37,43}$ and the N-terminal methionine is optional.

27. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln^{26}->Ala^{26} and the N-terminal methionine is optional.

28. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln^{174}->Ala^{174} and the N-terminal methionine is optional.

29. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Arg^{170}->Ala^{170} and the N-terminal methionine is optional.

30. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Arg^{167}->Ala^{167} and the N-terminal methionine is optional.

31. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that there is a deletion at position 167 and the N-terminal methionine is optional.

32. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys^{41}->Ala^{41} and the N-terminal methionine is optional.

33. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that His^{44}->Lys^{44} and the N-terminal methionine is optional.

34. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Glu^{47}->Ala^{47} and the N-terminal methionine is optional.

35. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Arg^{23}->Ala^{23} and the N-terminal methionine is optional.

36. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that

Lys^{24}->Ala^{24} and the N-terminal methionine is optional.

37. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Glu^{20}->Ala^{20} and the N-terminal methionine is optional.

38. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Asp^{28}->Ala^{28} and the N-terminal methionine is optional.

39. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Met^{127}->Glu^{127} and the N-terminal methionine is optional.

40. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from tha of Figure 1 in that Met^{138}->Glu^{138} and the N-terminal methionine is optional.

41. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Met^{127}->Leu^{127} and the N-terminal methionine is optional.

42. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Met^{138}->Leu^{138} and the N-terminal methionine is optional.

43. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Cys^{18}->Ala^{18} and the N-terminal methionine is optional.

44. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that $Gln^{12,21}$->$Glu^{12,21}$ and the N-terminal methionine is optional.

45. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino

acid sequence differs from that of Figure 1 in that $Gln^{12,21,68}$->$Glu^{12,21,68}$ and the N-terminal methionine is optional.

46. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Glu^{20}->Ala^{20}; Ser^{13}->Gly^{13} and the N-terminal methionine is optional.

47. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that $Met^{127,138}$->$Leu^{127,138}$ and the N-terminal methionine is optional.

48. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Ser^{13}->Ala^{13} and the N-terminal methionine is optional.

49. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Lys^{17}->Ala^{17} and the N-terminal methionine is optional.

50. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln^{121}->Ala^{121} and the N-terminal methionine is optional.

51. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Gln^{21}->Ala^{21} and the N-terminal methionine is optional.

52. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that His^{44}->Ala^{44} and the N-terminal methionine is optional.

53. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein said amino acid sequenc differs from that of Figure 1 in that

His^{53}->Ala^{53} and the N-terminal methionine is optional.

54. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Asp^{110}->Ala^{110} and the N-terminal methionine is optional.

55. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Asp^{113}->Ala^{113} and the N-terminal methionine is optional.

56. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Thr^{117}->Ala^{117} and the N-terminal methionine is optional.

57. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Asp^{28}->Ala^{28}; Asp^{110} ->Ala^{110} and the N-terminal methionine is optional.

58. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Glu^{124}->Ala^{124} and the N-terminal methionine is optional.

59. A G-CSF analog, optionally in a pharmaceutically effective carrier, wherein the amino acid sequence differs from that of Figure 1 in that Phe^{114}->Val^{114}, Thr^{117}->A^{117} and the N-terminal methionine is optional.

FIG.1

```
                                        Met Thr Pro Leu Gly Pro Ala
TCTAGAAAAAACCAAGGAGGTAATAAATA ATG ACT CCA TTA GGT CCT GCT

Ser Ser Leu Pro Gln Ser Phe Leu Leu Lys Cys Leu Glu Gln
TCT TCT CTG CCG CAA AGC TTT CTG CTG AAA TGT CTG GAA CAG

Val Arg Lys Ile Gln Gly Asp Gly Ala Ala Leu Gln Glu Lys Leu
GTT CGT AAA ATC CAG GGT GAC GGT GCT GCA CTG CAA GAA AAA CTG

Cys Ala Thr Tyr Lys Leu Cys His Pro Glu Glu Leu Val Leu Leu
TGC GCT ACT TAC AAA CTG TGC CAT CCG GAA GAG CTG GTA CTG CTG

Gly His Ser Leu Gly Ile Pro Trp Ala Pro Leu Ser Ser Cys Pro
GGT CAT TCT CTT GGG ATC CCG TGG GCT CCG CTG TCT TCT TGT CCA

Ser Gln Ala Leu Gln Leu Ala Gly Cys Leu Ser Gln Leu His Ser
TCT CAA GCT CTT CAG CTG GCT GGT TGT CTG TCT CAA CTG CAT TCT

Gly Leu Phe Leu Tyr Gln Gly Leu Leu Gln Ala Leu Glu Gly Ile
GGT CTG TTC CTG TAT CAG GGT CTT CTG CAA GCT CTG GAA GGT ATC

Ser Pro Glu Leu Gly Pro Thr Leu Asp Thr Leu Gln Leu Asp Val
TCT CCG GAA CTG GGT CCG ACT CTG GAC ACT CTG CAG CTA GAT GTA

Ala Asp Phe Ala Thr Thr Ile Trp Gln Gln Met Glu Glu Leu Gly
GCT GAC TTT GCT ACT ACT ATT TGG CAA CAG ATG GAA GAG CTC GGT

Met Ala Pro Ala Leu Gln Pro Thr Gln Gly Ala Met Pro Ala Phe
ATG GCA CCA GCT CTG CAA CCG ACT CAA GGT GCT ATG CCG GCA TTC

Ala Ser Ala Phe Gln Arg Arg Ala Gly Gly Val Leu Val Ala Ser
GCT TCT GCA TTC CAG CGT CGT GCA GGA GGT GTA CTG GTT GCT TCT

His Leu Gln Ser Phe Leu Glu Val Ser Tyr Arg Val Leu Arg His
CAT CTG CAA TCT TTC CTG GAA GTA TCT TAC CGT GTT CTG CGT CAT

Leu Ala Gln Pro OC  AM
CTG GCT CAG CCG TAA TAG AATTC
```

FIG. 2A
rhG-CSF

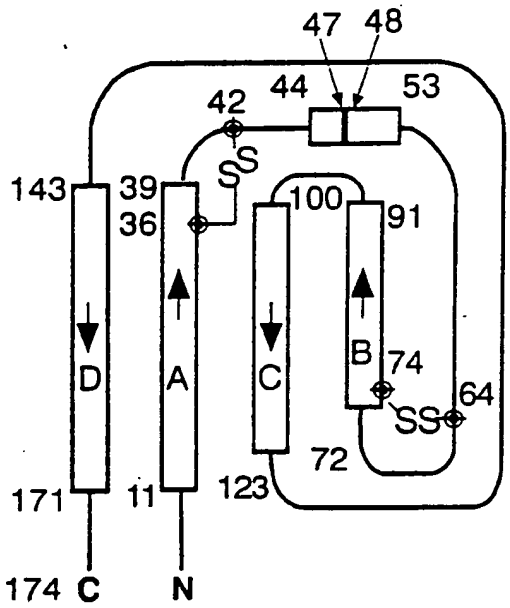

FIG. 2B
hGH

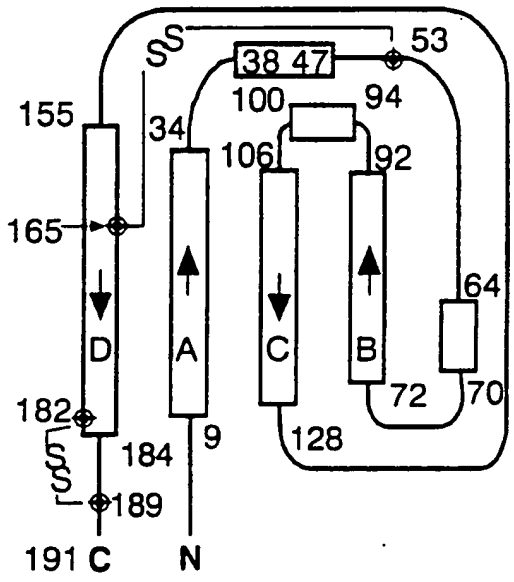

FIG. 2C
pGH

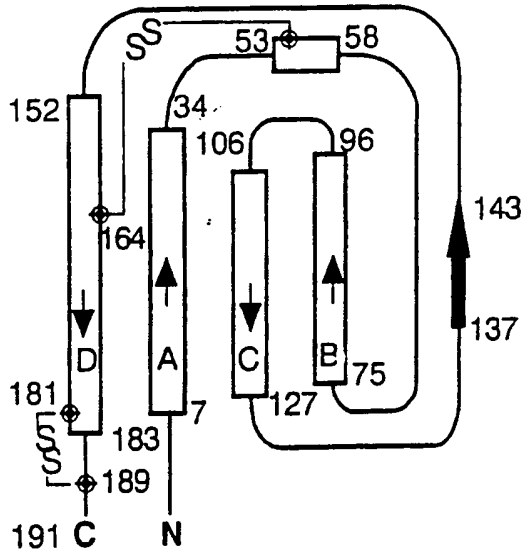

FIG. 2D
GM-CSF

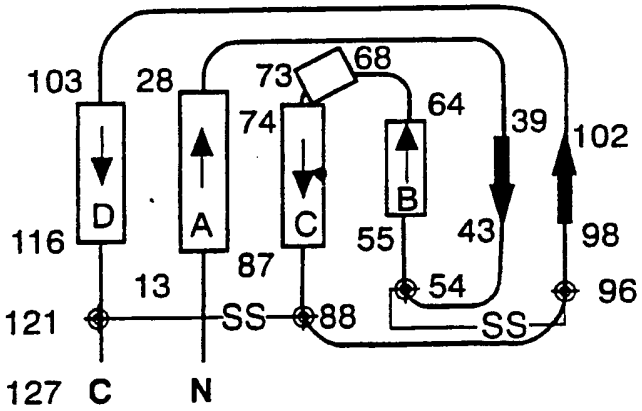

FIG. 2E
INF-B

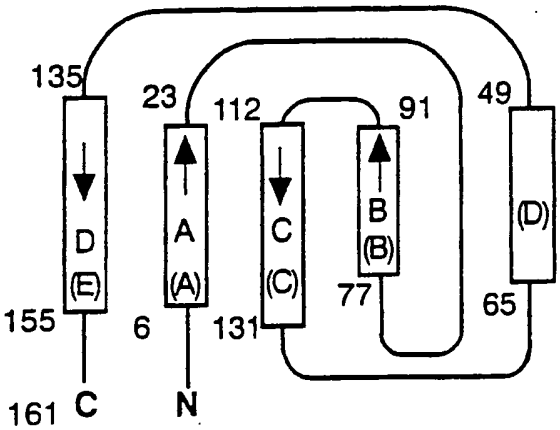

FIG. 2F
IL-2

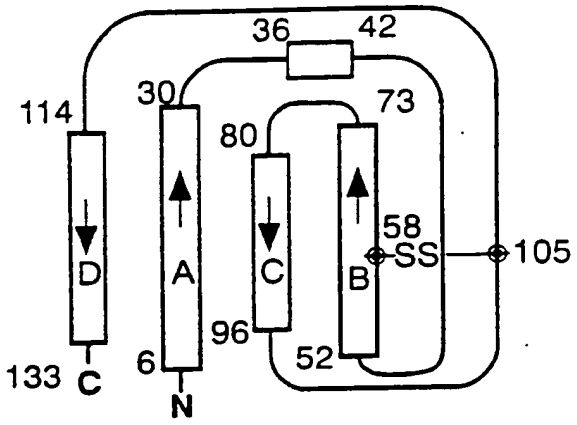

FIG. 2G
IL-4

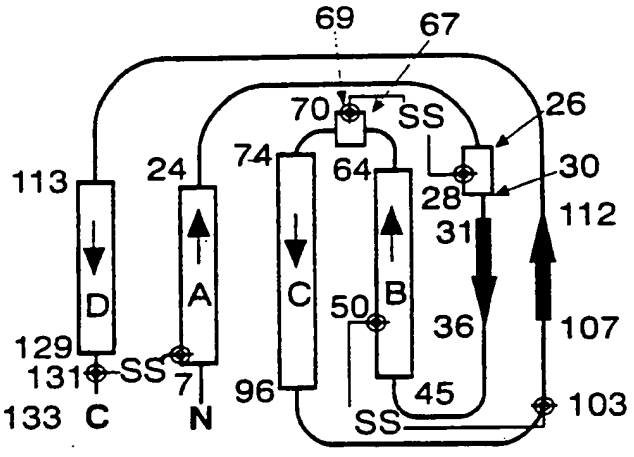

FIG. 3D FIG. 3C

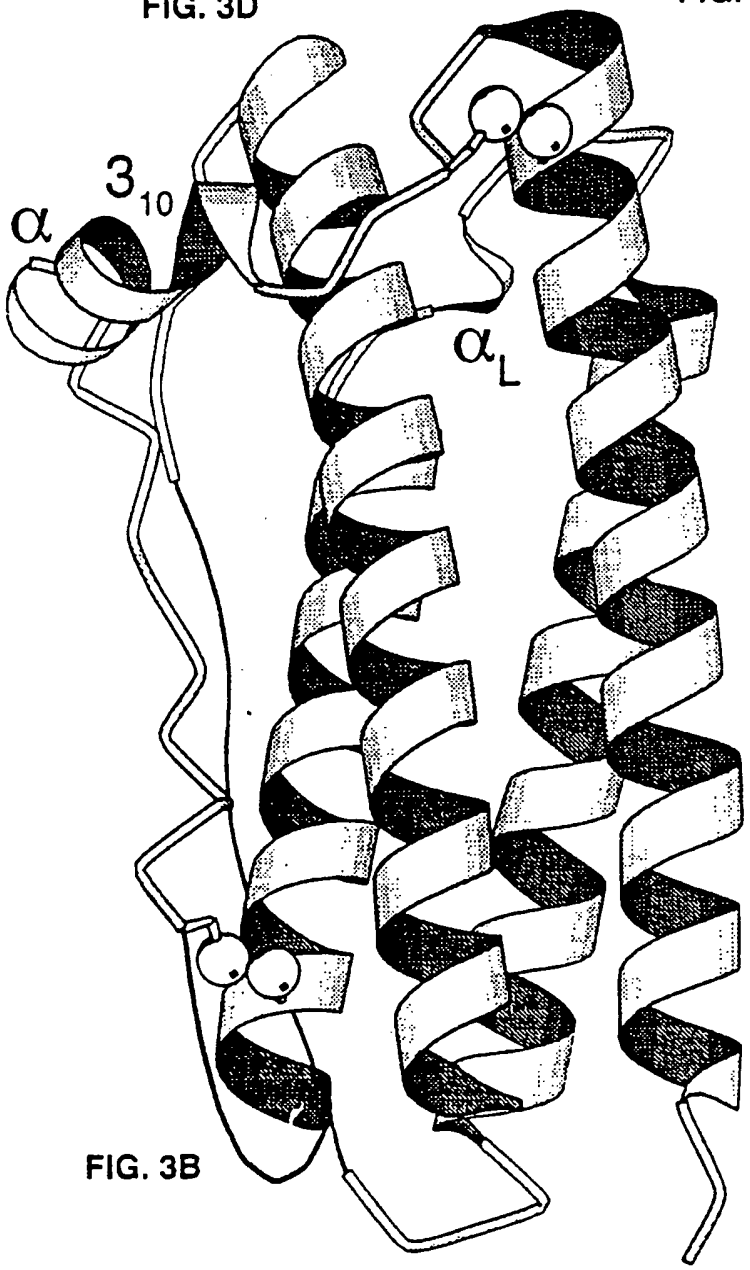

FIG. 3B FIG. 3A

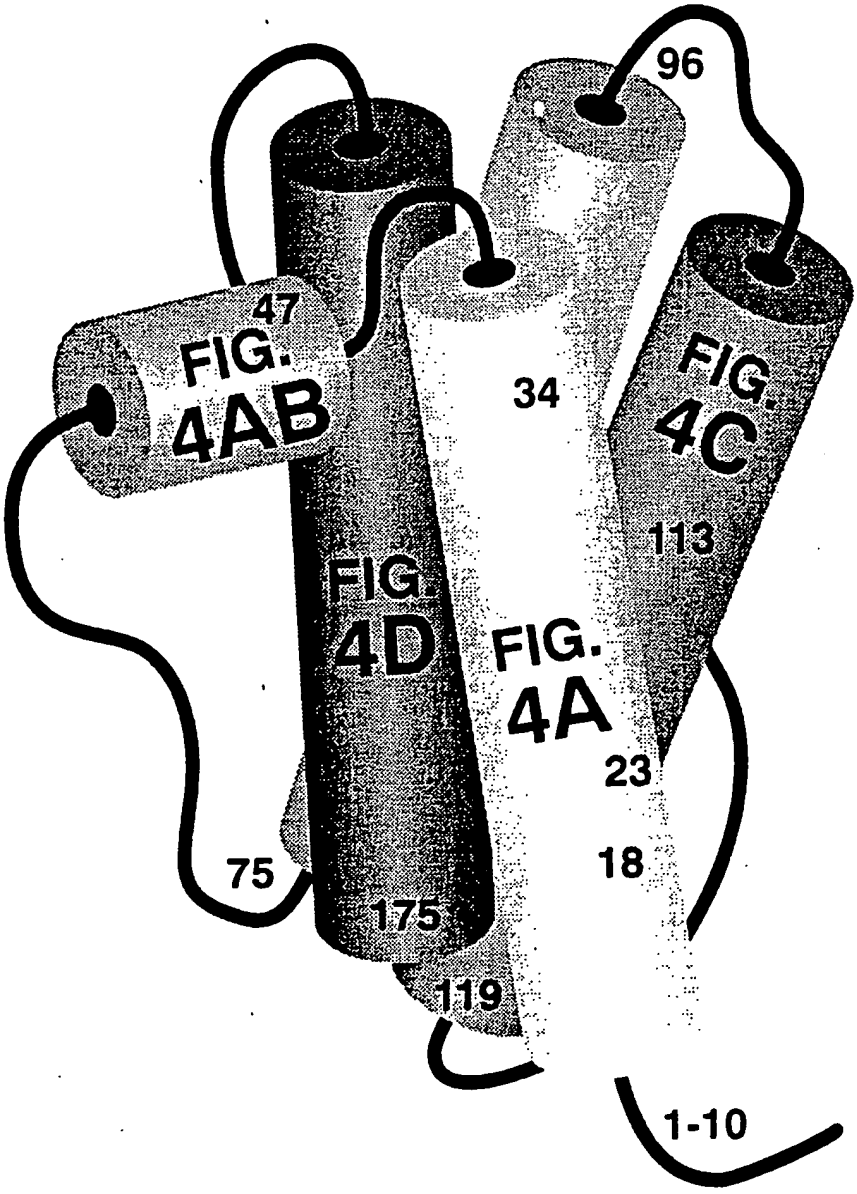
96
47
FIG. 4AB
34
FIG. 4C
113
FIG. 4D
FIG. 4A
23
18
75
175
119
1-10

FIG.5A

```
ATOM    1 CB  LEU  10    58.751  58.191 -14.868  1.00 61.22      A1
ATOM    2 CG  LEU  10    58.360  59.271 -13.939  1.00 60.19      A1
ATOM    3 CD1 LEU  10    59.307  60.461 -14.022  1.00 60.14      A1
ATOM    4 CD2 LEU  10    56.954  59.658 -14.335  1.00 60.68      A1
ATOM    5 C   LEU  10    60.544  56.734 -13.849  1.00 62.85      A1
ATOM    6 O   LEU  10    60.079  55.595 -14.0841  1.00 63.08      A1
ATOM    7 HT1 LEU  10    59.876  56.135 -15.998  1.00  0.00      A1
ATOM    8 HT2 LEU  10    61.323  56.887 -16.434  1.00  0.00      A1
ATOM    9 N   LEU  10    60.328  57.059 -16.204  1.00 62.24      A1
ATOM   10 HT3 LEU  10    59.817  57.535 -16.971  1.00  0.00      A1
ATOM   11 CA  LEU  10    60.183  57.758 -14.941  1.00 62.58      A1
ATOM   12 N   PRO  11    61.357  56.962 -12.780  1.00 61.96      A1
ATOM   13 CD  PRO  11    61.960  58.238 -12.383  1.00 61.21      A1
ATOM   14 CA  PRO  11    61.832  55.889 -11.906  1.00 61.34      A1
ATOM   15 CB  PRO  11    62.915  56.547 -11.043  1.00 59.77      A1
ATOM   16 CG  PRO  11    62.511  57.983 -10.975  1.00 59.16      A1
ATOM   17 C   PRO  11    60.712  55.225 -11.109  1.00 60.68      A1
ATOM   18 O   PRO  11    60.075  55.843 -10.250  1.00 61.73      A1
ATOM   19 N   GLN  12    60.466  53.946 -11.407  1.00 59.31      A1
ATOM   20 H   GLN  12    60.944  53.573 -12.175  1.00  0.00      A1
ATOM   21 CA  GLN  12    59.468  53.121 -10.743  1.00 57.22      A1
ATOM   22 CB  GLN  12    59.779  51.646 -10.970  1.00 59.27      A1
ATOM   23 CG  GLN  12    58.620  50.714 -10.591  1.00 59.70      A1
ATOM   24 CD  GLN  12    57.604  50.575 -11.702  1.00 61.71      A1
ATOM   25 OE1 GLN  12    57.170  49.465 -11.970  1.00 65.82      A1
ATOM   26 NE2 GLN  12    57.227  51.534 -12.541  1.00 63.02      A1
ATOM   27 HE21 GLN  12    57.639  52.419 -12.489  1.00  0.00      A1
ATOM   28 HE22 GLN  12    56.500  51.308 -13.156  1.00  0.00      A1
ATOM   29 C   GLN  12    59.336  53.347  -9.245  1.00 55.34      A1
ATOM   30 O   GLN  12    58.242  53.196  -8.708  1.00 54.56      A1
ATOM   31 N   SER  13    60.423  53.732  -8.576  1.00 53.44      A1
ATOM   32 H   SER  13    61.276  53.839  -9.033  1.00  0.00      A1
ATOM   33 CA  SER  13    60.335  53.974  -7.168  1.00 52.86      A1
ATOM   34 CB  SER  13    61.704  54.144  -6.626  1.00 52.24      A1
ATOM   35 OG  SER  13    61.702  53.493  -5.362  1.00 56.64      A1
ATOM   36 HG  SER  13    61.534  52.551  -5.477  1.00  0.00      A1
ATOM   37 C   SER  13    59.497  55.214  -6.900  1.00 52.58      A1
ATOM   38 O   SER  13    58.509  55.144  -6.160  1.00 53.55      A1
ATOM   39 N   PHE  14    59.791  56.333  -7.577  1.00 50.84      A1
ATOM   40 H   PHE  14    60.469  56.292  -8.279  1.00  0.00      A1
ATOM   41 CA  PHE  14    59.067  57.590  -7.423  1.00 47.21      A1
ATOM   42 CB  PHE  14    59.611  58.590  -8.454  1.00 44.68      A1
ATOM   43 CG  PHE  14    58.618  59.669  -8.866  1.00 42.88      A1
ATOM   44 CD1 PHE  14    58.052  59.594 -10.123  1.00 40.40      A1
ATOM   45 CD2 PHE  14    58.264  60.673  -7.978  1.00 40.30      A1
ATOM   46 CE1 PHE  14    57.114  60.518 -10.507  1.00 39.59      A1
ATOM   47 CE2 PHE  14    57.329  61.587  -8.380  1.00 41.82      A1
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ATOM   50 O   PHE  14    56.789  57.588  -6.805  1.00 46.07      A1
ATOM   51 N   LEU  15    57.298  56.509  -8.718  1.00 44.64      A1
ATOM   52 H   LEU  15    58.024  56.183  -9.287  1.00  0.00      A1
ATOM   53 CA  LEU  15    55.940  56.181  -9.038  1.00 44.53      A1
ATOM   54 CB  LEU  15    55.858  55.402 -10.300  1.00 48.74      A1
ATOM   55 CG  LEU  15    54.853  56.013 -11.289  1.00 51.65      A1
ATOM   56 CD1 LEU  15    55.525  57.121 -12.105  1.00 50.33      A1
ATOM   57 CD2 LEU  15    54.320  54.906 -12.204  1.00 53.77      A1
ATOM   58 C   LEU  15    55.169  55.410  -8.014  1.00 44.07      A1
ATOM   59 O   LEU  15    53.945  55.567  -7.959  1.00 45.46      A1
ATOM   60 N   LEU  16    55.809  54.620  -7.166  1.00 43.18      A1
ATOM   61 H   LEU  16    56.781  54.503  -7.251  1.00  0.00      A1
ATOM   62 CA  LEU  16    55.110  53.913  -6.095  1.00 42.96      A1
ATOM   63 CB  LEU  16    55.866  52.623  -5.751  1.00 43.34      A1
ATOM   64 CG  LEU  16    55.840  51.608  -6.868  1.00 42.25      A1
ATOM   65 CD1 LEU  16    56.889  50.567  -6.596  1.00 43.68      A1
ATOM   66 CD2 LEU  16    54.413  51.068  -7.030  1.00 42.75      A1
ATOM   67 C   LEU  16    54.963  54.778  -4.852  1.00 42.35      A1
ATOM   68 O   LEU  16    54.077  54.579  -4.018  1.00 42.65      A1
ATOM   69 N   LYS  17    55.823  55.779  -4.703  1.00 42.47      A1
ATOM   70 H   LYS  17    56.587  55.840  -5.320  1.00  0.00      A1
```

FIG.5B

```
ATOM   71 CA  LYS  17      55.681  56.767  -3.650  1.00 42.07      A1
ATOM   72 CB  LYS  17      56.995  57.554  -3.573  1.00 44.14      A1
ATOM   73 CG  LYS  17      57.214  58.197  -2.223  1.00 49.61      A1
ATOM   74 CD  LYS  17      57.114  57.164  -1.086  1.00 55.15      A1
ATOM   75 CE  LYS  17      56.747  57.804   0.293  1.00 62.05      A1
ATOM   76 NZ  LYS  17      55.462  58.533   0.331  1.00 65.43      A1
ATOM   77 HZ1 LYS  17      54.684  57.884   0.098  1.00  0.00      A1
ATOM   78 HZ2 LYS  17      55.482  59.308  -0.362  1.00  0.00      A1
ATOM   79 HZ3 LYS  17      55.312  58.926   1.282  1.00  0.00      A1
ATOM   80 C   LYS  17      54.463  57.640  -4.051  1.00 41.20      A1
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ATOM   82 N   CYS  18      54.272  57.992  -5.346  1.00 39.13      A1
ATOM   83 H   CYS  18      54.998  57.809  -5.981  1.00  0.00      A1
ATOM   84 CA  CYS  18      53.080  58.656  -5.802  1.00 37.42      A1
ATOM   85 CB  CYS  18      53.092  58.891  -7.261  1.00 35.02      A1
ATOM   86 SG  CYS  18      54.421  60.026  -7.681  1.00 40.40      A1
ATOM   87 C   CYS  18      51.859  57.789  -5.502  1.00 39.33      A1
ATOM   88 O   CYS  18      50.959  58.346  -4.847  1.00 40.83      A1
ATOM   89 N   LEU  19      51.738  56.475  -5.842  1.00 37.15      A1
ATOM   90 H   LEU  19      52.462  56.038  -6.341  1.00  0.00      A1
ATOM   91 CA  LEU  19      50.521  55.702  -5.534  1.00 36.00      A1
ATOM   92 CB  LEU  19      50.644  54.204  -5.947  1.00 38.31      A1
ATOM   93 CG  LEU  19      49.410  53.271  -5.657  1.00 40.86      A1
ATOM   94 CD1 LEU  19      48.208  53.684  -6.467  1.00 39.71      A1
ATOM   95 CD2 LEU  19      49.692  51.833  -6.113  1.00 45.71      A1
ATOM   96 C   LEU  19      50.102  55.736  -4.076  1.00 33.52      A1
ATOM   97 O   LEU  19      48.930  55.949  -3.766  1.00 32.75      A1
ATOM   98 N   GLU  20      51.030  55.576  -3.166  1.00 31.88      A1
ATOM   99 H   GLU  20      51.940  55.338  -3.455  1.00  0.00      A1
ATOM  100 CA  GLU  20      50.750  55.710  -1.748  1.00 33.40      A1
ATOM  101 CB  GLU  20      52.053  55.334  -1.167  1.00 35.25      A1
ATOM  102 CG  GLU  20      52.508  55.504   0.260  1.00 43.21      A1
ATOM  103 CD  GLU  20      53.948  54.947   0.407  1.00 51.06      A1
ATOM  104 OE1 GLU  20      54.320  54.660   1.546  1.00 56.78      A1
ATOM  105 OE2 GLU  20      54.708  54.766  -0.570  1.00 51.57      A1
ATOM  106 C   GLU  20      50.230  57.117  -1.326  1.00 33.25      A1
ATOM  107 O   GLU  20      49.432  57.291  -0.380  1.00 33.30      A1
ATOM  108 N   GLN  21      50.660  58.167  -2.044  1.00 32.33      A1
ATOM  109 H   GLN  21      51.270  58.004  -2.794  1.00  0.00      A1
ATOM  110 CA  GLN  21      50.275  59.538  -1.742  1.00 31.00      A1
ATOM  111 CB  GLN  21      51.326  60.489  -2.340  1.00 32.37      A1
ATOM  112 CG  GLN  21      52.436  60.530  -1.272  1.00 38.01      A1
ATOM  113 CD  GLN  21      53.622  61.460  -1.504  1.00 42.67      A1
ATOM  114 OE1 GLN  21      54.008  62.236  -0.615  1.00 43.63      A1
ATOM  115 NE2 GLN  21      54.256  61.448  -2.678  1.00 42.31      A1
ATOM  116 HE21 GLN  21      53.965  60.840  -3.384  1.00  0.00      A1
ATOM  117 HE22 GLN  21      55.026  62.052  -2.730  1.00  0.00      A1
ATOM  118 C   GLN  21      48.894  59.765  -2.288  1.00 28.51      A1
ATOM  119 O   GLN  21      48.027  60.242  -1.563  1.00 28.65      A1
ATOM  120 N   VAL  22      48.682  59.319  -3.521  1.00 25.85      A1
ATOM  121 H   VAL  22      49.448  58.980  -4.013  1.00  0.00      A1
ATOM  122 CA  VAL  22      47.382  59.303  -4.161  1.00 24.94      A1
ATOM  123 CB  VAL  22      47.508  58.614  -5.526  1.00 24.09      A1
ATOM  124 CG1 VAL  22      46.154  58.378  -6.096  1.00 19.97      A1
ATOM  125 CG2 VAL  22      48.252  59.479  -6.498  1.00 25.82      A1
ATOM  126 C   VAL  22      46.418  58.549  -3.226  1.00 25.65      A1
ATOM  127 O   VAL  22      45.428  59.190  -2.800  1.00 29.31      A1
ATOM  128 N   ARG  23      46.643  57.291  -2.759  1.00 23.93      A1
ATOM  129 H   ARG  23      47.440  56.819  -3.056  1.00  0.00      A1
ATOM  130 CA  ARG  23      45.667  56.593  -1.892  1.00 20.67      A1
ATOM  131 CB  ARG  23      46.104  55.135  -1.635  1.00 20.45      A1
ATOM  132 CG  ARG  23      46.325  54.321  -2.904  1.00 17.51      A1
ATOM  133 CD  ARG  23      45.095  54.446  -3.769  1.00 21.54      A1
ATOM  134 NE  ARG  23      45.076  53.437  -4.809  1.00 24.82      A1
ATOM  135 HE  ARG  23      45.642  52.647  -4.701  1.00  0.00      A1
ATOM  136 CZ  ARG  23      44.323  53.556  -5.904  1.00 27.69      A1
ATOM  137 NH1 ARG  23      43.567  54.669  -6.006  1.00 29.51      A1
ATOM  138 HH11 ARG  23      43.562  55.377  -5.303  1.00  0.00      A1
ATOM  139 HH12 ARG  23      42.956  54.730  -6.789  1.00  0.00      A1
ATOM  140 NH2 ARG  23      44.345  52.604  -6.891  1.00 24.22      A1
ATOM  141 HH21 ARG  23      43.780  52.713  -7.709  1.00  0.00      A1
ATOM  142 HH22 ARG  23      44.936  51.802  -6.793  1.00  0.00      A1
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FIG.5C

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ATOM  143 C   ARG  23    45.458 57.285 -0.560 1.00 20.56   A1
ATOM  144 O   ARG  23    44.374 57.254  0.042 1.00 20.04   A1
ATOM  145 N   LYS  24    46.485 58.015 -0.118 1.00 22.67   A1
ATOM  146 H   LYS  24    47.291 58.105 -0.668 1.00  0.00   A1
ATOM  147 CA  LYS  24    46.431 58.729  1.166 1.00 22.85   A1
ATOM  148 CB  LYS  24    47.811 59.255  1.506 1.00 26.86   A1
ATOM  149 CG  LYS  24    47.821 59.661  2.971 1.00 33.79   A1
ATOM  150 CD  LYS  24    49.121 60.265  3.404 1.00 40.73   A1
ATOM  151 CE  LYS  24    50.258 59.258  3.335 1.00 46.19   A1
ATOM  152 NZ  LYS  24    51.532 59.975  3.333 1.00 51.19   A1
ATOM  153 HZ1 LYS  24    51.637 60.498  4.225 1.00  0.00   A1
ATOM  154 HZ2 LYS  24    51.539 60.651  2.539 1.00  0.00   A1
ATOM  155 HZ3 LYS  24    52.317 59.303  3.216 1.00  0.00   A1
ATOM  156 C   LYS  24    45.455 59.893  1.101 1.00 21.66   A1
ATOM  157 O   LYS  24    44.588 60.068  1.962 1.00 20.90   A1
ATOM  158 N   ILE  25    45.549 60.696  0.044 1.00 21.66   A1
ATOM  159 H   ILE  25    46.242 60.509 -0.629 1.00  0.00   A1
ATOM  160 CA  ILE  25    44.667 61.841 -0.115 1.00 22.53   A1
ATOM  161 CB  ILE  25    45.075 62.694 -1.307 1.00 22.15   A1
ATOM  162 CG2 ILE  25    44.097 63.834 -1.439 1.00 20.44   A1
ATOM  163 CG1 ILE  25    46.475 63.230 -1.136 1.00 21.03   A1
ATOM  164 CD  ILE  25    47.188 63.281 -2.497 1.00 20.03   A1
ATOM  165 C   ILE  25    43.263 61.308 -0.352 1.00 24.75   A1
ATOM  166 O   ILE  25    42.339 61.839  0.301 1.00 26.13   A1
ATOM  167 N   GLN  26    43.065 60.289 -1.244 1.00 22.79   A1
ATOM  168 H   GLN  26    43.842 59.926 -1.726 1.00  0.00   A1
ATOM  169 CA  GLN  26    41.737 59.713 -1.437 1.00 20.12   A1
ATOM  170 CB  GLN  26    41.729 58.539 -2.341 1.00 18.89   A1
ATOM  171 CG  GLN  26    42.203 59.042 -3.627 1.00 19.77   A1
ATOM  172 CD  GLN  26    42.163 57.996 -4.684 1.00 24.26   A1
ATOM  173 OE1 GLN  26    42.550 56.853 -4.465 1.00 26.82   A1
ATOM  174 NE2 GLN  26    41.732 58.351 -5.890 1.00 27.68   A1
ATOM  175 HE21 GLN 26    41.421 59.265 -6.042 1.00  0.00   A1
ATOM  176 HE22 GLN 26    41.743 57.649 -6.552 1.00  0.00   A1
ATOM  177 C   GLN  26    41.207 59.239 -0.111 1.00 21.88   A1
ATOM  178 O   GLN  26    40.067 59.550  0.220 1.00 27.02   A1
ATOM  179 N   GLY  27    41.952 58.622  0.773 1.00 22.54   A1
ATOM  180 H   GLY  27    42.891 58.420  0.576 1.00  0.00   A1
ATOM  181 CA  GLY  27    41.386 58.191  2.037 1.00 25.55   A1
ATOM  182 C   GLY  27    40.936 59.352  2.890 1.00 27.80   A1
ATOM  183 O   GLY  27    39.889 59.251  3.526 1.00 29.95   A1
ATOM  184 N   ASP  28    41.683 60.460  2.915 1.00 29.39   A1
ATOM  185 H   ASP  28    42.547 60.454  2.448 1.00  0.00   A1
ATOM  186 CA  ASP  28    41.257 61.680  3.624 1.00 28.45   A1
ATOM  187 CB  ASP  28    42.266 62.789  3.552 1.00 30.13   A1
ATOM  188 CG  ASP  28    43.737 62.502  3.777 1.00 31.72   A1
ATOM  189 OD1 ASP  28    44.539 63.024  2.995 1.00 31.95   A1
ATOM  190 OD2 ASP  28    44.063 61.811  4.741 1.00 32.00   A1
ATOM  191 C   ASP  28    39.994 62.264  2.960 1.00 25.81   A1
ATOM  192 O   ASP  28    39.101 62.699  3.655 1.00 26.21   A1
ATOM  193 N   GLY  29    39.882 62.270  1.631 1.00 23.93   A1
ATOM  194 H   GLY  29    40.660 61.950  1.135 1.00  0.00   A1
ATOM  195 CA  GLY  29    38.729 62.694  0.886 1.00 25.69   A1
ATOM  196 C   GLY  29    37.528 61.961  1.418 1.00 27.36   A1
ATOM  197 O   GLY  29    36.648 62.558  2.061 1.00 28.14   A1
ATOM  198 N   ALA  30    37.646 60.628  1.295 1.00 27.85   A1
ATOM  199 H   ALA  30    38.442 60.288  0.843 1.00  0.00   A1
ATOM  200 CA  ALA  30    36.683 59.655  1.814 1.00 25.94   A1
ATOM  201 CB  ALA  30    37.269 58.303  1.556 1.00 22.15   A1
ATOM  202 C   ALA  30    36.356 59.842  3.308 1.00 27.18   A1
ATOM  203 O   ALA  30    35.194 59.772  3.754 1.00 28.82   A1
ATOM  204 N   ALA  31    37.340 60.105  4.150 1.00 27.16   A1
ATOM  205 H   ALA  31    38.253 60.114  3.809 1.00  0.00   A1
ATOM  206 CA  ALA  31    37.113 60.470  5.531 1.00 27.70   A1
ATOM  207 CB  ALA  31    38.383 60.881  6.177 1.00 27.65   A1
ATOM  208 C   ALA  31    36.178 61.675  5.660 1.00 30.01   A1
ATOM  209 O   ALA  31    35.195 61.624  6.413 1.00 32.91   A1
ATOM  210 N   LEU  32    36.397 62.744  4.895 1.00 27.63   A1
ATOM  211 H   LEU  32    37.133 62.734  4.242 1.00  0.00   A1
ATOM  212 CA  LEU  32    35.560 63.898  4.997 1.00 28.52   A1
ATOM  213 CB  LEU  32    36.226 65.019  4.167 1.00 32.94   A1
ATOM  214 CG  LEU  32    35.658 66.472  4.091 1.00 32.54   A1
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FIG.5D

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ATOM  215 CD1 LEU  32    35.516 67.082  5.499 1.00 32.87    A1
ATOM  216 CD2 LEU  32    36.555 67.267  3.181 1.00 30.97    A1
ATOM  217 C   LEU  32    34.133 63.597  4.518 1.00 27.87    A1
ATOM  218 O   LEU  32    33.169 63.889  5.250 1.00 25.93    A1
ATOM  219 N   GLN  33    33.977 63.028  3.315 1.00 27.51    A1
ATOM  220 H   GLN  33    34.787 62.826  2.802 1.00  0.00    A1
ATOM  221 CA  GLN  33    32.687 62.671  2.775 1.00 30.40    A1
ATOM  222 CB  GLN  33    32.737 61.721  1.614 1.00 29.47    A1
ATOM  223 CG  GLN  33    32.888 62.584  0.436 1.00 29.26    A1
ATOM  224 CD  GLN  33    33.015 61.869 -0.887 1.00 30.21    A1
ATOM  225 OE1 GLN  33    34.064 61.495 -1.452 1.00 29.61    A1
ATOM  226 NE2 GLN  33    31.823 61.759 -1.426 1.00 33.19    A1
ATOM  227 HE21 GLN  33    31.781 61.328 -2.302 1.00  0.00    A1
ATOM  228 HE22 GLN  33    31.042 62.060 -0.914 1.00  0.00    A1
ATOM  229 C   GLN  33    31.839 61.963  3.788 1.00 35.60    A1
ATOM  230 O   GLN  33    30.715 62.416  4.073 1.00 36.49    A1
ATOM  231 N   GLU  34    32.386 60.925  4.438 1.00 39.81    A1
ATOM  232 H   GLU  34    33.340 60.707  4.328 1.00  0.00    A1
ATOM  233 CA  GLU  34    31.541 60.131  5.304 1.00 43.24    A1
ATOM  234 CB  GLU  34    32.228 58.792  5.571 1.00 46.46    A1
ATOM  235 CG  GLU  34    33.274 58.721  6.624 1.00 55.01    A1
ATOM  236 CD  GLU  34    32.777 58.092  7.930 1.00 60.29    A1
ATOM  237 OE1 GLU  34    33.483 57.186  8.412 1.00 63.26    A1
ATOM  238 OE2 GLU  34    31.724 58.504  8.459 1.00 60.44    A1
ATOM  239 C   GLU  34    31.218 60.877  6.564 1.00 43.59    A1
ATOM  240 O   GLU  34    30.175 60.631  7.161 1.00 44.87    A1
ATOM  241 N   LYS  35    32.045 61.811  6.998 1.00 44.80    A1
ATOM  242 H   LYS  35    32.923 61.931  6.569 1.00  0.00    A1
ATOM  243 CA  LYS  35    31.674 62.634  8.134 1.00 45.43    A1
ATOM  244 CB  LYS  35    32.881 63.364  8.686 1.00 47.67    A1
ATOM  245 CG  LYS  35    33.701 62.414  9.510 1.00 52.75    A1
ATOM  246 CD  LYS  35    35.084 63.021  9.548 1.00 57.55    A1
ATOM  247 CE  LYS  35    36.067 62.099 10.238 1.00 60.35    A1
ATOM  248 NZ  LYS  35    35.810 62.064 11.669 1.00 62.91    A1
ATOM  249 HZ1 LYS  35    34.838 61.733 11.840 1.00  0.00    A1
ATOM  250 HZ2 LYS  35    35.930 63.011 12.078 1.00  0.00    A1
ATOM  251 HZ3 LYS  35    36.477 61.405 12.119 1.00  0.00    A1
ATOM  252 C   LYS  35    30.630 63.660  7.697 1.00 44.45    A1
ATOM  253 O   LYS  35    29.730 63.999  8.478 1.00 44.61    A1
ATOM  254 N   LEU  36    30.652 64.190  6.480 1.00 41.21    A1
ATOM  255 H   LEU  36    31.343 63.930  5.836 1.00  0.00    A1
ATOM  256 CA  LEU  36    29.647 65.157  6.144 1.00 40.25    A1
ATOM  257 CB  LEU  36    30.070 65.899  4.889 1.00 39.03    A1
ATOM  258 CG  LEU  36    31.253 66.834  4.935 1.00 33.99    A1
ATOM  259 CD1 LEU  36    31.438 67.404  3.571 1.00 32.08    A1
ATOM  260 CD2 LEU  36    31.034 67.939  5.928 1.00 35.05    A1
ATOM  261 C   LEU  36    28.332 64.414  5.941 1.00 41.90    A1
ATOM  262 O   LEU  36    27.267 64.828  6.431 1.00 42.30    A1
ATOM  263 N   CYS  37    28.392 63.251  5.309 1.00 42.63    A1
ATOM  264 H   CYS  37    29.250 62.904  5.020 1.00  0.00    A1
ATOM  265 CA  CYS  37    27.216 62.469  5.084 1.00 43.53    A1
ATOM  266 C   CYS  37    26.638 62.026  6.362 1.00 44.65    A1
ATOM  267 O   CYS  37    25.426 61.997  6.459 1.00 46.40    A1
ATOM  268 CB  CYS  37    27.474 61.240  4.313 1.00 44.60    A1
ATOM  269 SG  CYS  37    26.133 60.038  4.530 1.00 43.86    A1
ATOM  270 N   ALA  38    27.465 61.734  7.342 1.00 45.96    A1
ATOM  271 H   ALA  38    28.433 61.707  7.202 1.00  0.00    A1
ATOM  272 CA  ALA  38    26.932 61.261  8.592 1.00 48.03    A1
ATOM  273 CB  ALA  38    27.869 60.140  9.108 1.00 48.64    A1
ATOM  274 C   ALA  38    26.748 62.358  9.624 1.00 48.89    A1
ATOM  275 O   ALA  38    26.103 62.085 10.621 1.00 50.72    A1
ATOM  276 N   THR  39    27.256 63.590  9.512 1.00 50.66    A1
ATOM  277 H   THR  39    27.858 63.780  8.770 1.00  0.00    A1
ATOM  278 CA  THR  39    26.976 64.638 10.503 1.00 51.54    A1
ATOM  279 CB  THR  39    28.179 65.593 10.690 1.00 51.76    A1
ATOM  280 OG1 THR  39    29.294 64.826 11.126 1.00 52.65    A1
ATOM  281 HG1 THR  39    29.749 64.481 10.355 1.00  0.00    A1
ATOM  282 CG2 THR  39    27.900 66.655 11.729 1.00 51.62    A1
ATOM  283 C   THR  39    25.775 65.466 10.037 1.00 52.17    A1
ATOM  284 O   THR  39    24.886 65.882 10.781 1.00 52.15    A1
ATOM  285 N   TYR  40    25.751 65.720  8.738 1.00 52.83    A1
ATOM  286 H   TYR  40    26.420 65.331  8.139 1.00  0.00    A1
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FIG.5E

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ATOM  287 CA  TYR  40    24.729 66.561  8.165 1.00 52.53    A1
ATOM  288 CB  TYR  40    25.314 67.872  7.696 1.00 52.15    A1
ATOM  289 CG  TYR  40    26.399 68.458  8.552 1.00 54.11    A1
ATOM  290 CD1 TYR  40    27.678 68.341  8.062 1.00 56.50    A1
ATOM  291 CE1 TYR  40    28.719 68.934  8.724 1.00 58.28    A1
ATOM  292 CD2 TYR  40    26.122 69.144  9.714 1.00 54.86    A1
ATOM  293 CE2 TYR  40    27.170 69.746 10.378 1.00 56.20    A1
ATOM  294 CZ  TYR  40    28.453 69.642  9.872 1.00 58.26    A1
ATOM  295 OH  TYR  40    29.513 70.310 10.463 1.00 61.00    A1
ATOM  296 HH  TYR  40    30.179 70.443  9.782 1.00  0.00    A1
ATOM  297 C   TYR  40    24.035 65.911  6.981 1.00 51.75    A1
ATOM  298 O   TYR  40    23.662 66.578  6.024 1.00 52.52    A1
ATOM  299 N   LYS  41    23.941 64.600  6.965 1.00 50.54    A1
ATOM  300 H   LYS  41    24.474 64.064  7.583 1.00  0.00    A1
ATOM  301 CA  LYS  41    23.112 63.885  6.029 1.00 50.48    A1
ATOM  302 CB  LYS  41    21.641 63.989  6.540 1.00 50.62    A1
ATOM  303 CG  LYS  41    21.387 63.326  7.911 1.00 52.11    A1
ATOM  304 CD  LYS  41    20.112 63.878  8.574 1.00 55.54    A1
ATOM  305 CE  LYS  41    19.578 63.087  9.820 1.00 58.79    A1
ATOM  306 NZ  LYS  41    18.374 63.648 10.457 1.00 58.31    A1
ATOM  307 HZ1 LYS  41    17.605 63.688  9.757 1.00  0.00    A1
ATOM  308 HZ2 LYS  41    18.578 64.607 10.803 1.00  0.00    A1
ATOM  309 HZ3 LYS  41    18.084 63.043 11.252 1.00  0.00    A1
ATOM  310 C   LYS  41    23.251 64.318  4.588 1.00 49.92    A1
ATOM  311 O   LYS  41    22.312 64.124  3.793 1.00 51.49    A1
ATOM  312 N   LEU  42    24.432 64.893  4.246 1.00 48.28    A1
ATOM  313 H   LEU  42    25.103 65.050  4.937 1.00  0.00    A1
ATOM  314 CA  LEU  42    24.742 65.286  2.859 1.00 46.61    A1
ATOM  315 CB  LEU  42    25.565 66.574  2.757 1.00 44.69    A1
ATOM  316 CG  LEU  42    24.807 67.802  3.218 1.00 42.63    A1
ATOM  317 CD1 LEU  42    25.718 68.580  4.097 1.00 43.29    A1
ATOM  318 CD2 LEU  42    24.283 68.590  2.045 1.00 41.26    A1
ATOM  319 C   LEU  42    25.580 64.124  2.397 1.00 45.46    A1
ATOM  320 O   LEU  42    26.766 64.017  2.711 1.00 46.32    A1
ATOM  321 N   CYS  43    24.882 63.193  1.754 1.00 44.09    A1
ATOM  322 H   CYS  43    23.925 63.353  1.619 1.00  0.00    A1
ATOM  323 CA  CYS  43    25.480 61.951  1.358 1.00 42.87    A1
ATOM  324 C   CYS  43    25.448 61.846 -0.123 1.00 41.62    A1
ATOM  325 O   CYS  43    25.762 60.805 -0.666 1.00 41.99    A1
ATOM  326 CB  CYS  43    24.716 60.796  2.026 1.00 41.77    A1
ATOM  327 SG  CYS  43    24.523 61.011  3.835 1.00 45.91    A1
ATOM  328 N   HIS  44    25.057 62.846 -0.882 1.00 42.90    A1
ATOM  329 H   HIS  44    24.841 63.721 -0.491 1.00  0.00    A1
ATOM  330 CA  HIS  44    25.069 62.680 -2.320 1.00 44.60    A1
ATOM  331 CB  HIS  44    23.653 62.264 -2.825 1.00 48.40    A1
ATOM  332 CG  HIS  44    23.085 60.935 -2.310 1.00 50.37    A1
ATOM  333 CD2 HIS  44    22.178 60.844 -1.272 1.00 50.52    A1
ATOM  334 ND1 HIS  44    23.358 59.689 -2.713 1.00 52.28    A1
ATOM  335 HD1 HIS  44    24.130 59.394 -3.251 1.00  0.00    A1
ATOM  336 CE1 HIS  44    22.652 58.873 -1.955 1.00 51.92    A1
ATOM  337 NE2 HIS  44    21.947 59.565 -1.091 1.00 50.53    A1
ATOM  338 HE2 HIS  44    21.290 59.189 -0.466 1.00  0.00    A1
ATOM  339 C   HIS  44    25.522 63.941 -3.047 1.00 43.69    A1
ATOM  340 O   HIS  44    24.765 64.906 -3.108 1.00 43.00    A1
ATOM  341 N   PRO  45    26.710 63.978 -3.667 1.00 43.07    A1
ATOM  342 CD  PRO  45    27.785 62.995 -3.501 1.00 42.17    A1
ATOM  343 CA  PRO  45    27.133 65.024 -4.570 1.00 42.50    A1
ATOM  344 CB  PRO  45    28.380 64.466 -5.217 1.00 39.76    A1
ATOM  345 CG  PRO  45    28.995 63.680 -4.123 1.00 39.09    A1
ATOM  346 C   PRO  45    26.071 65.423 -5.585 1.00 44.49    A1
ATOM  347 O   PRO  45    25.876 66.612 -5.801 1.00 45.36    A1
ATOM  348 N   GLU  46    25.334 64.501 -6.225 1.00 45.36    A1
ATOM  349 H   GLU  46    25.464 63.561 -5.996 1.00  0.00    A1
ATOM  350 CA  GLU  46    24.406 64.806 -7.319 1.00 45.46    A1
ATOM  351 CB  GLU  46    23.952 63.515 -7.997 1.00 50.54    A1
ATOM  352 CG  GLU  46    24.462 63.460 -9.445 1.00 58.48    A1
ATOM  353 CD  GLU  46    23.637 64.215 -10.502 1.00 64.93    A1
ATOM  354 OE1 GLU  46    23.642 65.455 -10.516 1.00 68.55    A1
ATOM  355 OE2 GLU  46    22.995 63.554 -11.332 1.00 68.31    A1
ATOM  356 C   GLU  46    23.181 65.584 -6.937 1.00 42.96    A1
ATOM  357 O   GLU  46    22.532 66.223 -7.748 1.00 41.71    A1
ATOM  358 N   GLU  47    22.919 65.563 -5.654 1.00 41.96    A1
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FIG.5F

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ATOM  359 H   GLU  47    23.507 65.098 -5.028 1.00 0.00    A1
ATOM  360 CA  GLU  47    21.818 66.301 -5.144 1.00 43.21   A1
ATOM  361 CB  GLU  47    21.294 65.487 -3.963 1.00 43.24   A1
ATOM  362 CG  GLU  47    21.409 65.925 -2.515 1.00 46.07   A1
ATOM  363 CD  GLU  47    20.812 64.907 -1.547 1.00 47.86   A1
ATOM  364 OE1 GLU  47    19.847 64.225 -1.910 1.00 50.99   A1
ATOM  365 OE2 GLU  47    21.313 64.780 -0.427 1.00 49.47   A1
ATOM  366 C   GLU  47    22.295 67.718 -4.809 1.00 44.04   A1
ATOM  367 O   GLU  47    21.532 68.547 -4.292 1.00 44.60   A1
ATOM  368 N   LEU  48    23.567 68.015 -5.121 1.00 43.05   A1
ATOM  369 H   LEU  48    24.140 67.310 -5.465 1.00 0.00    A1
ATOM  370 CA  LEU  48    24.166 69.318 -4.904 1.00 42.42   A1
ATOM  371 CB  LEU  48    25.223 69.201 -3.858 1.00 40.53   A1
ATOM  372 CG  LEU  48    24.920 68.695 -2.489 1.00 41.87   A1
ATOM  373 CD1 LEU  48    26.277 68.424 -1.892 1.00 41.71   A1
ATOM  374 CD2 LEU  48    24.096 69.670 -1.633 1.00 41.13   A1
ATOM  375 C   LEU  48    24.792 69.937 -6.166 1.00 42.37   A1
ATOM  376 O   LEU  48    25.439 70.994 -6.098 1.00 42.37   A1
ATOM  377 N   VAL  49    24.566 69.366 -7.347 1.00 41.52   A1
ATOM  378 H   VAL  49    23.951 68.602 -7.362 1.00 0.00    A1
ATOM  379 CA  VAL  49    25.191 69.822 -8.578 1.00 43.34   A1
ATOM  380 CB  VAL  49    24.890 68.761 -9.636 1.00 44.29   A1
ATOM  381 CG1 VAL  49    23.381 68.709 -9.830 1.00 47.50   A1
ATOM  382 CG2 VAL  49    25.540 69.086 -10.975 1.00 45.25  A1
ATOM  383 C   VAL  49    24.740 71.214 -9.028 1.00 44.98   A1
ATOM  384 O   VAL  49    25.401 71.901 -9.814 1.00 46.03   A1
ATOM  385 N   LEU  50    23.565 71.602 -8.530 1.00 46.16   A1
ATOM  386 H   LEU  50    23.081 70.933 -8.006 1.00 0.00    A1
ATOM  387 CA  LEU  50    22.908 72.895 -8.729 1.00 46.03   A1
ATOM  388 CB  LEU  50    21.469 72.769 -8.264 1.00 46.43   A1
ATOM  389 CG  LEU  50    20.443 73.718 -8.760 1.00 44.16   A1
ATOM  390 CD1 LEU  50    20.259 73.558 -10.243 1.00 44.79  A1
ATOM  391 CD2 LEU  50    19.159 73.400 -8.079 1.00 44.66   A1
ATOM  392 C   LEU  50    23.632 73.968 -7.917 1.00 45.85   A1
ATOM  393 O   LEU  50    23.996 74.989 -8.484 1.00 44.52   A1
ATOM  394 N   LEU  51    23.853 73.764 -6.606 1.00 45.44   A1
ATOM  395 H   LEU  51    23.489 72.958 -6.189 1.00 0.00    A1
ATOM  396 CA  LEU  51    24.676 74.656 -5.805 1.00 46.04   A1
ATOM  397 CB  LEU  51    24.860 74.084 -4.435 1.00 45.53   A1
ATOM  398 CG  LEU  51    25.741 74.931 -3.535 1.00 47.78   A1
ATOM  399 CD1 LEU  51    25.148 76.320 -3.322 1.00 47.13   A1
ATOM  400 CD2 LEU  51    25.902 74.202 -2.219 1.00 48.33   A1
ATOM  401 C   LEU  51    26.064 74.845 -6.436 1.00 46.27   A1
ATOM  402 O   LEU  51    26.551 75.966 -6.612 1.00 47.62   A1
ATOM  403 N   GLY  52    26.702 73.736 -6.809 1.00 44.84   A1
ATOM  404 H   GLY  52    26.306 72.869 -6.578 1.00 0.00    A1
ATOM  405 CA  GLY  52    27.989 73.758 -7.453 1.00 42.91   A1
ATOM  406 C   GLY  52    27.984 74.533 -8.750 1.00 42.47   A1
ATOM  407 O   GLY  52    28.853 75.364 -8.983 1.00 42.06   A1
ATOM  408 N   HIS  53    27.047 74.307 -9.653 1.00 42.02   A1
ATOM  409 H   HIS  53    26.366 73.624 -9.471 1.00 0.00    A1
ATOM  410 CA  HIS  53    27.009 75.104 -10.861 1.00 42.23  A1
ATOM  411 CB  HIS  53    25.842 74.689 -11.706 1.00 42.21  A1
ATOM  412 CG  HIS  53    26.076 73.399 -12.460 1.00 44.60  A1
ATOM  413 CD2 HIS  53    25.112 72.774 -13.200 1.00 47.49  A1
ATOM  414 ND1 HIS  53    27.180 72.669 -12.578 1.00 46.76  A1
ATOM  415 HD1 HIS  53    28.039 72.853 -12.139 1.00 0.00   A1
ATOM  416 CE1 HIS  53    26.954 71.641 -13.346 1.00 46.90  A1
ATOM  417 NE2 HIS  53    25.704 71.725 -13.707 1.00 50.22  A1
ATOM  418 HE2 HIS  53    25.237 71.033 -14.239 1.00 0.00   A1
ATOM  419 C   HIS  53    26.893 76.585 -10.536 1.00 42.72   A1
ATOM  420 O   HIS  53    27.622 77.399 -11.068 1.00 42.03   A1
ATOM  421 N   SER  54    26.099 76.920 -9.535 1.00 45.08   A1
ATOM  422 H   SER  54    25.673 76.218 -9.001 1.00 0.00    A1
ATOM  423 CA  SER  54    25.792 78.278 -9.177 1.00 46.92   A1
ATOM  424 CB  SER  54    24.576 78.181 -8.289 1.00 48.86   A1
ATOM  425 OG  SER  54    23.521 77.616 -9.112 1.00 53.06   A1
ATOM  426 HG  SER  54    23.465 76.677 -8.918 1.00 0.00    A1
ATOM  427 C   SER  54    26.939 79.033 -8.549 1.00 47.92   A1
ATOM  428 O   SER  54    27.038 80.264 -8.655 1.00 49.60   A1
ATOM  429 N   LEU  55    27.837 78.273 -7.933 1.00 47.59   A1
ATOM  430 H   LEU  55    27.638 77.322 -7.791 1.00 0.00    A1
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FIG.5G

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ATOM  431 CA  LEU  55     29.075 78.810 -7.401  1.00 45.27      A1
ATOM  432 CB  LEU  55     29.552 77.913 -6.243  1.00 45.49      A1
ATOM  433 CG  LEU  55     28.840 77.992 -4.874  1.00 47.30      A1
ATOM  434 CD1 LEU  55     28.876 76.596 -4.299  1.00 49.52      A1
ATOM  435 CD2 LEU  55     29.530 78.921 -3.862  1.00 45.69      A1
ATOM  436 C   LEU  55     30.133 78.889 -8.492  1.00 43.63      A1
ATOM  437 O   LEU  55     31.247 79.350 -8.272  1.00 43.24      A1
ATOM  438 N   GLY  56     29.855 78.383 -9.675  1.00 43.55      A1
ATOM  439 H   GLY  56     28.984 77.975 -9.828  1.00  0.00      A1
ATOM  440 CA  GLY  56     30.814 78.390 -10.753 1.00 45.59      A1
ATOM  441 C   GLY  56     32.182 77.811 -10.392 1.00 46.76      A1
ATOM  442 O   GLY  56     33.171 78.213 -11.015 1.00 47.31      A1
ATOM  443 N   ILE  57     32.247 76.885 -9.412  1.00 47.49      A1
ATOM  444 H   ILE  57     31.392 76.594 -9.042  1.00  0.00      A1
ATOM  445 CA  ILE  57     33.486 76.249 -8.950  1.00 48.28      A1
ATOM  446 CB  ILE  57     33.144 75.172 -7.863  1.00 47.79      A1
ATOM  447 CG2 ILE  57     34.457 74.591 -7.348  1.00 46.85      A1
ATOM  448 CG1 ILE  57     32.338 75.764 -6.701  1.00 45.09      A1
ATOM  449 CD  ILE  57     31.859 74.739 -5.659  1.00 41.23      A1
ATOM  450 C   ILE  57     34.276 75.602 -10.115 1.00 49.15      A1
ATOM  451 O   ILE  57     33.678 74.935 -10.968 1.00 49.04      A1
ATOM  452 N   PRO  58     35.596 75.817 -10.248 1.00 49.75      A1
ATOM  453 CD  PRO  58     36.402 76.743 -9.433  1.00 50.94      A1
ATOM  454 CA  PRO  58     36.421 75.228 -11.302 1.00 50.72      A1
ATOM  455 CB  PRO  58     37.525 76.241 -11.488 1.00 50.92      A1
ATOM  456 CG  PRO  58     37.814 76.663 -10.041 1.00 50.82      A1
ATOM  457 C   PRO  58     36.916 73.845 -10.875 1.00 50.36      A1
ATOM  458 O   PRO  58     37.187 73.599 -9.691  1.00 49.75      A1
ATOM  459 N   TRP  59     37.030 72.927 -11.816 1.00 50.37      A1
ATOM  460 H   TRP  59     36.888 73.141 -12.760 1.00  0.00      A1
ATOM  461 CA  TRP  59     37.524 71.595 -11.482 1.00 51.78      A1
ATOM  462 CB  TRP  59     36.435 70.562 -11.857 1.00 49.06      A1
ATOM  463 CG  TRP  59     35.254 70.712 -10.889 1.00 46.37      A1
ATOM  464 CD2 TRP  59     35.320 70.845 -9.521  1.00 44.06      A1
ATOM  465 CE2 TRP  59     33.998 71.027 -9.205  1.00 44.18      A1
ATOM  466 CE3 TRP  59     36.274 70.842 -8.538  1.00 44.03      A1
ATOM  467 CD1 TRP  59     33.972 70.794 -11.354 1.00 45.17      A1
ATOM  468 NE1 TRP  59     33.229 70.994 -10.297 1.00 43.17      A1
ATOM  469 HE1 TRP  59     32.301 71.312 -10.332 1.00  0.00      A1
ATOM  470 CZ2 TRP  59     33.598 71.215 -7.916  1.00 45.60      A1
ATOM  471 CZ3 TRP  59     35.893 71.028 -7.243  1.00 45.25      A1
ATOM  472 CH2 TRP  59     34.565 71.214 -6.938  1.00 46.43      A1
ATOM  473 C   TRP  59     38.815 71.435 -12.256 1.00 52.84      A1
ATOM  474 O   TRP  59     38.842 71.972 -13.372 1.00 54.96      A1
ATOM  475 N   ALA  60     39.912 70.834 -11.777 1.00 51.97      A1
ATOM  476 H   ALA  60     39.857 70.269 -10.977 1.00  0.00      A1
ATOM  477 CA  ALA  60     41.108 70.870 -12.609 1.00 52.18      A1
ATOM  478 CB  ALA  60     42.303 70.610 -11.748 1.00 51.75      A1
ATOM  479 C   ALA  60     41.055 69.857 -13.746 1.00 52.16      A1
ATOM  480 O   ALA  60     40.545 68.760 -13.530 1.00 52.17      A1
ATOM  481 N   PRO  61     41.435 70.145 -14.986 1.00 53.34      A1
ATOM  482 CD  PRO  61     41.370 71.458 -15.622 1.00 54.76      A1
ATOM  483 CA  PRO  61     41.691 69.145 -15.993 1.00 55.57      A1
ATOM  484 CB  PRO  61     41.792 69.918 -17.310 1.00 54.95      A1
ATOM  485 CG  PRO  61     42.211 71.297 -16.901 1.00 54.05      A1
ATOM  486 C   PRO  61     42.934 68.333 -15.690 1.00 57.54      A1
ATOM  487 O   PRO  61     43.757 68.661 -14.834 1.00 57.20      A1
ATOM  488 N   LEU  62     43.040 67.271 -16.486 1.00 59.98      A1
ATOM  489 H   LEU  62     42.285 67.067 -17.077 1.00  0.00      A1
ATOM  490 CA  LEU  62     44.184 66.370 -16.471 1.00 63.64      A1
ATOM  491 CB  LEU  62     44.062 65.417 -15.260 1.00 63.72      A1
ATOM  492 CG  LEU  62     45.323 64.691 -14.865 1.00 64.43      A1
ATOM  493 CD1 LEU  62     46.394 65.704 -14.488 1.00 64.02      A1
ATOM  494 CD2 LEU  62     45.016 63.764 -13.717 1.00 64.98      A1
ATOM  495 C   LEU  62     44.214 65.611 -17.812 1.00 65.69      A1
ATOM  496 OT1 LEU  62     44.256 66.302 -18.844 1.00 68.47      A1
ATOM  497 OT2 LEU  62     44.194 64.371 -17.845 1.00 66.57      A1
ATOM  498 CB  LEU  72     57.448 63.159 -19.422 1.00 63.44      A2
ATOM  499 CG  LEU  72     57.716 62.495 -18.117 1.00 63.40      A2
ATOM  500 CD1 LEU  72     56.719 61.408 -17.913 1.00 61.50      A2
ATOM  501 CD2 LEU  72     59.107 61.901 -18.121 1.00 63.22      A2
ATOM  502 C   LEU  72     55.897 65.084 -18.876 1.00 65.40      A2
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FIG.5H

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ATOM  503 O   LEU  72   54.827 65.301 -18.316 1.00 67.30   A2
ATOM  504 HT1 LEU  72   56.469 64.683 -21.261 1.00  0.00   A2
ATOM  505 HT2 LEU  72   54.827 64.355 -20.951 1.00  0.00   A2
ATOM  506 N   LEU  72   55.795 63.983 -20.899 1.00 66.29   A2
ATOM  507 HT3 LEU  72   55.866 63.098 -21.439 1.00  0.00   A2
ATOM  508 CA  LEU  72   56.064 63.714 -19.512 1.00 64.91   A2
ATOM  509 N   ALA  73   56.807 66.046 -19.086 1.00 64.54   A2
ATOM  510 H   ALA  73   57.690 65.804 -19.432 1.00  0.00   A2
ATOM  511 CA  ALA  73   56.707 67.433 -18.615 1.00 62.55   A2
ATOM  512 CB  ALA  73   57.553 68.314 -19.529 1.00 64.84   A2
ATOM  513 C   ALA  73   55.319 68.024 -18.539 1.00 60.37   A2
ATOM  514 O   ALA  73   54.801 68.180 -17.456 1.00 59.42   A2
ATOM  515 N   GLY  74   54.693 68.226 -19.691 1.00 59.72   A2
ATOM  516 H   GLY  74   55.212 68.174 -20.514 1.00  0.00   A2
ATOM  517 CA  GLY  74   53.336 68.728 -19.816 1.00 59.99   A2
ATOM  518 C   GLY  74   52.327 68.114 -18.865 1.00 60.27   A2
ATOM  519 O   GLY  74   51.880 68.796 -17.935 1.00 60.80   A2
ATOM  520 N   CYS  75   51.945 66.850 -19.030 1.00 59.60   A2
ATOM  521 H   CYS  75   52.160 66.358 -19.839 1.00  0.00   A2
ATOM  522 CA  CYS  75   51.002 66.276 -18.078 1.00 60.17   A2
ATOM  523 CB  CYS  75   50.670 64.801 -18.464 1.00 64.08   A2
ATOM  524 SG  CYS  75   49.832 64.732 -20.096 1.00 73.47   A2
ATOM  525 C   CYS  75   51.502 66.346 -16.642 1.00 56.73   A2
ATOM  526 O   CYS  75   50.734 66.748 -15.765 1.00 55.82   A2
ATOM  527 N   LEU  76   52.795 66.142 -16.396 1.00 53.93   A2
ATOM  528 H   LEU  76   53.423 66.043 -17.137 1.00  0.00   A2
ATOM  529 CA  LEU  76   53.325 66.156 -15.044 1.00 52.94   A2
ATOM  530 CB  LEU  76   54.798 65.754 -15.181 1.00 50.81   A2
ATOM  531 CG  LEU  76   55.575 65.011 -14.090 1.00 49.02   A2
ATOM  532 CD1 LEU  76   54.852 63.740 -13.698 1.00 46.76   A2
ATOM  533 CD2 LEU  76   56.951 64.633 -14.623 1.00 47.67   A2
ATOM  534 C   LEU  76   53.093 67.545 -14.425 1.00 53.65   A2
ATOM  535 O   LEU  76   52.731 67.716 -13.244 1.00 53.50   A2
ATOM  536 N   SER  77   53.137 68.553 -15.301 1.00 53.91   A2
ATOM  537 H   SER  77   53.322 68.361 -16.242 1.00  0.00   A2
ATOM  538 CA  SER  77   52.882 69.932 -14.942 1.00 54.93   A2
ATOM  539 CB  SER  77   53.425 70.835 -16.040 1.00 58.32   A2
ATOM  540 OG  SER  77   54.806 70.587 -16.310 1.00 63.35   A2
ATOM  541 HG  SER  77   54.949 69.637 -16.315 1.00  0.00   A2
ATOM  542 C   SER  77   51.382 70.172 -14.759 1.00 53.47   A2
ATOM  543 O   SER  77   50.982 70.965 -13.899 1.00 53.54   A2
ATOM  544 N   GLN  78   50.509 69.501 -15.512 1.00 51.82   A2
ATOM  545 H   GLN  78   50.857 68.901 -16.207 1.00  0.00   A2
ATOM  546 CA  GLN  78   49.074 69.619 -15.349 1.00 50.74   A2
ATOM  547 CB  GLN  78   48.402 68.877 -16.451 1.00 54.31   A2
ATOM  548 CG  GLN  78   47.420 69.784 -17.160 1.00 58.59   A2
ATOM  549 CD  GLN  78   46.557 68.940 -18.071 1.00 62.32   A2
ATOM  550 OE1 GLN  78   47.005 68.260 -18.998 1.00 65.94   A2
ATOM  551 NE2 GLN  78   45.269 68.889 -17.800 1.00 63.17   A2
ATOM  552 HE21 GLN  78   44.973 69.327 -16.972 1.00  0.00   A2
ATOM  553 HE22 GLN  78   44.704 68.444 -18.456 1.00  0.00   A2
ATOM  554 C   GLN  78   48.591 69.065 -14.011 1.00 48.17   A2
ATOM  555 O   GLN  78   47.691 69.618 -13.368 1.00 46.31   A2
ATOM  556 N   LEU  79   49.236 67.988 -13.564 1.00 45.89   A2
ATOM  557 H   LEU  79   49.920 67.584 -14.140 1.00  0.00   A2
ATOM  558 CA  LEU  79   48.919 67.359 -12.294 1.00 44.54   A2
ATOM  559 CB  LEU  79   49.617 66.015 -12.259 1.00 45.06   A2
ATOM  560 CG  LEU  79   49.154 64.895 -11.351 1.00 45.18   A2
ATOM  561 CD1 LEU  79   49.634 63.594 -11.957 1.00 48.06   A2
ATOM  562 CD2 LEU  79   49.766 64.986 -9.969 1.00 46.03   A2
ATOM  563 C   LEU  79   49.366 68.265 -11.170 1.00 43.49   A2
ATOM  564 O   LEU  79   48.645 68.509 -10.199 1.00 43.20   A2
ATOM  565 N   HIS  80   50.556 68.834 -11.329 1.00 43.83   A2
ATOM  566 H   HIS  80   51.115 68.548 -12.085 1.00  0.00   A2
ATOM  567 CA  HIS  80   51.060 69.788 -10.360 1.00 43.79   A2
ATOM  568 CB  HIS  80   52.456 70.221 -10.810 1.00 43.58   A2
ATOM  569 CG  HIS  80   53.030 71.031 -9.690 1.00 43.75   A2
ATOM  570 CD2 HIS  80   53.484 70.497 -8.517 1.00 47.48   A2
ATOM  571 ND1 HIS  80   53.083 72.343 -9.567 1.00 44.24   A2
ATOM  572 HD1 HIS  80   52.842 73.004 -10.255 1.00  0.00   A2
ATOM  573 CE1 HIS  80   53.530 72.641 -8.376 1.00 44.47   A2
ATOM  574 NE2 HIS  80   53.772 71.520 -7.748 1.00 48.16   A2
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FIG.5I

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ATOM  575 HE2 HIS  80     54.103 71.444 -6.824 1.00 0.00     A2
ATOM  576 C  HIS  80     50.094 70.978 -10.229 1.00 44.40   A2
ATOM  577 O  HIS  80     49.643 71.294 -9.131 1.00 44.28    A2
ATOM  578 N  SER  81     49.733 71.670 -11.309 1.00 45.13   A2
ATOM  579 H  SER  81     50.136 71.459 -12.176 1.00 0.00    A2
ATOM  580 CA SER  81     48.738 72.742 -11.296 1.00 45.41   A2
ATOM  581 CB SER  81     48.612 73.347 -12.682 1.00 45.59   A2
ATOM  582 OG SER  81     49.894 73.444 -13.292 1.00 49.27   A2
ATOM  583 HG SER  81     50.058 72.670 -13.843 1.00 0.00    A2
ATOM  584 C  SER  81     47.344 72.266 -10.856 1.00 44.85   A2
ATOM  585 O  SER  81     46.604 73.064 -10.256 1.00 46.83   A2
ATOM  586 N  GLY  82     46.946 71.010 -11.092 1.00 42.16   A2
ATOM  587 H  GLY  82     47.513 70.411 -11.614 1.00 0.00    A2
ATOM  588 CA GLY  82     45.663 70.500 -10.650 1.00 39.39   A2
ATOM  589 C  GLY  82     45.569 70.461 -9.139 1.00 39.30    A2
ATOM  590 O  GLY  82     44.542 70.843 -8.544 1.00 39.64    A2
ATOM  591 N  LEU  83     46.676 70.032 -8.521 1.00 37.57    A2
ATOM  592 H  LEU  83     47.413 69.695 -9.075 1.00 0.00     A2
ATOM  593 CA LEU  83     46.826 70.007 -7.057 1.00 38.07    A2
ATOM  594 CB LEU  83     48.133 69.202 -6.748 1.00 35.67    A2
ATOM  595 CG LEU  83     48.071 67.736 -7.225 1.00 32.51    A2
ATOM  596 CD1 LEU  83    49.442 67.145 -7.319 1.00 29.77    A2
ATOM  597 CD2 LEU  83    47.180 66.973 -6.288 1.00 28.71    A2
ATOM  598 C  LEU  83     46.836 71.386 -6.354 1.00 38.48    A2
ATOM  599 O  LEU  83     46.392 71.627 -5.219 1.00 38.05    A2
ATOM  600 N  PHE  84     47.366 72.338 -7.108 1.00 40.34    A2
ATOM  601 H  PHE  84     47.804 72.078 -7.944 1.00 0.00     A2
ATOM  602 CA PHE  84     47.414 73.703 -6.688 1.00 41.54    A2
ATOM  603 CB PHE  84     48.163 74.531 -7.693 1.00 46.88    A2
ATOM  604 CG PHE  84     48.715 75.777 -6.988 1.00 55.09    A2
ATOM  605 CD1 PHE  84    49.521 75.622 -5.849 1.00 55.31    A2
ATOM  606 CD2 PHE  84    48.396 77.053 -7.469 1.00 55.79    A2
ATOM  607 CE1 PHE  84    50.004 76.737 -5.195 1.00 57.60    A2
ATOM  608 CE2 PHE  84    48.892 78.156 -6.796 1.00 57.25    A2
ATOM  609 CZ PHE  84     49.688 78.002 -5.667 1.00 58.34    A2
ATOM  610 C  PHE  84     45.994 74.191 -6.591 1.00 40.47    A2
ATOM  611 O  PHE  84     45.609 74.749 -5.558 1.00 42.71    A2
ATOM  612 N  LEU  85     45.190 73.953 -7.624 1.00 38.64    A2
ATOM  613 H  LEU  85     45.555 73.527 -8.429 1.00 0.00     A2
ATOM  614 CA LEU  85     43.794 74.335 -7.584 1.00 38.81    A2
ATOM  615 CB LEU  85     43.101 73.886 -8.839 1.00 41.27    A2
ATOM  616 CG LEU  85     41.673 74.403 -9.017 1.00 46.45    A2
ATOM  617 CD1 LEU  85    41.702 75.784 -9.719 1.00 47.80    A2
ATOM  618 CD2 LEU  85    40.860 73.359 -9.787 1.00 48.25    A2
ATOM  619 C  LEU  85     43.079 73.731 -6.386 1.00 38.20    A2
ATOM  620 O  LEU  85     42.498 74.469 -5.582 1.00 38.36    A2
ATOM  621 N  TYR  86     43.150 72.405 -6.198 1.00 37.92    A2
ATOM  622 H  TYR  86     43.637 71.850 -6.845 1.00 0.00     A2
ATOM  623 CA TYR  86     42.501 71.801 -5.057 1.00 37.15    A2
ATOM  624 CB TYR  86     42.598 70.255 -5.102 1.00 36.73    A2
ATOM  625 CG TYR  86     41.561 69.685 -6.081 1.00 33.66    A2
ATOM  626 CD1 TYR  86    41.946 69.312 -7.374 1.00 30.03    A2
ATOM  627 CE1 TYR  86    40.991 68.885 -8.280 1.00 30.08    A2
ATOM  628 CD2 TYR  86    40.224 69.623 -5.666 1.00 32.61    A2
ATOM  629 CE2 TYR  86    39.263 69.203 -6.574 1.00 31.66    A2
ATOM  630 CZ TYR  86     39.656 68.838 -7.868 1.00 30.57    A2
ATOM  631 OH TYR  86     38.670 68.428 -8.751 1.00 28.18    A2
ATOM  632 HH TYR  86     39.107 67.994 -9.485 1.00 0.00     A2
ATOM  633 C  TYR  86     43.054 72.318 -3.746 1.00 37.75    A2
ATOM  634 O  TYR  86     42.173 72.469 -2.889 1.00 39.52    A2
ATOM  635 N  GLN  87     44.347 72.655 -3.478 1.00 36.93    A2
ATOM  636 H  GLN  87     45.044 72.463 -4.140 1.00 0.00     A2
ATOM  637 CA GLN  87     44.749 73.332 -2.205 1.00 36.40    A2
ATOM  638 CB GLN  87     46.210 73.668 -2.255 1.00 39.56    A2
ATOM  639 CG GLN  87     47.126 72.993 -1.237 1.00 46.99    A2
ATOM  640 CD GLN  87     48.641 73.062 -1.576 1.00 50.96    A2
ATOM  641 OE1 GLN  87    49.144 72.623 -2.627 1.00 52.15    A2
ATOM  642 NE2 GLN  87    49.446 73.608 -0.663 1.00 52.96    A2
ATOM  643 HE21 GLN  87   49.055 73.957 0.164 1.00 0.00      A2
ATOM  644 HE22 GLN  87   50.396 73.621 -0.888 1.00 0.00     A2
ATOM  645 C  GLN  87     43.941 74.652 -2.013 1.00 34.36    A2
ATOM  646 O  GLN  87     43.414 74.990 -0.935 1.00 31.55    A2
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FIG.5J

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ATOM  647 N   GLY  88   43.740 75.335 -3.159 1.00 32.73   A2
ATOM  648 H   GLY  88   44.165 75.005 -3.981 1.00  0.00   A2
ATOM  649 CA  GLY  88   42.948 76.546 -3.232 1.00 30.81   A2
ATOM  650 C   GLY  88   41.540 76.275 -2.731 1.00 30.47   A2
ATOM  651 O   GLY  88   41.130 76.819 -1.703 1.00 30.27   A2
ATOM  652 N   LEU  89   40.802 75.387 -3.406 1.00 29.01   A2
ATOM  653 H   LEU  89   41.220 74.912 -4.154 1.00  0.00   A2
ATOM  654 CA  LEU  89   39.447 75.102 -3.009 1.00 27.60   A2
ATOM  655 CB  LEU  89   38.922 74.073 -3.935 1.00 28.13   A2
ATOM  656 CG  LEU  89   38.764 74.583 -5.340 1.00 29.51   A2
ATOM  657 CD1 LEU  89   38.363 73.530 -6.364 1.00 24.13   A2
ATOM  658 CD2 LEU  89   37.673 75.637 -5.220 1.00 32.87   A2
ATOM  659 C   LEU  89   39.352 74.629 -1.583 1.00 29.88   A2
ATOM  660 O   LEU  89   38.427 75.012 -0.860 1.00 30.81   A2
ATOM  661 N   LEU  90   40.317 73.839 -1.094 1.00 32.59   A2
ATOM  662 H   LEU  90   41.101 73.626 -1.643 1.00  0.00   A2
ATOM  663 CA  LEU  90   40.182 73.274  0.235 1.00 33.41   A2
ATOM  664 CB  LEU  90   41.207 72.234  0.503 1.00 36.15   A2
ATOM  665 CG  LEU  90   41.075 70.971 -0.343 1.00 38.76   A2
ATOM  666 CD1 LEU  90   42.431 70.267 -0.456 1.00 37.21   A2
ATOM  667 CD2 LEU  90   39.995 70.099  0.279 1.00 40.54   A2
ATOM  668 C   LEU  90   40.342 74.319  1.255 1.00 34.24   A2
ATOM  669 O   LEU  90   39.711 74.256  2.313 1.00 35.57   A2
ATOM  670 N   GLN  91   41.188 75.291  0.940 1.00 35.24   A2
ATOM  671 H   GLN  91   41.663 75.284  0.078 1.00  0.00   A2
ATOM  672 CA  GLN  91   41.397 76.373  1.883 1.00 37.60   A2
ATOM  673 CB  GLN  91   42.557 77.182  1.363 1.00 39.65   A2
ATOM  674 CG  GLN  91   43.155 78.237  2.284 1.00 44.32   A2
ATOM  675 CD  GLN  91   44.348 78.799  1.542 1.00 46.96   A2
ATOM  676 OE1 GLN  91   45.235 78.083  1.068 1.00 47.42   A2
ATOM  677 NE2 GLN  91   44.376 80.092  1.341 1.00 46.82   A2
ATOM  678 HE21 GLN  91   43.690 80.685  1.700 1.00  0.00   A2
ATOM  679 HE22 GLN  91   45.108 80.331  0.741 1.00  0.00   A2
ATOM  680 C   GLN  91   40.129 77.231  2.061 1.00 37.22   A2
ATOM  681 O   GLN  91   39.718 77.530  3.186 1.00 36.21   A2
ATOM  682 N   ALA  92   39.456 77.570  0.943 1.00 38.63   A2
ATOM  683 H   ALA  92   39.808 77.205  0.098 1.00  0.00   A2
ATOM  684 CA  ALA  92   38.243 78.402  0.880 1.00 38.10   A2
ATOM  685 CB  ALA  92   37.657 78.436 -0.511 1.00 36.76   A2
ATOM  686 C   ALA  92   37.139 77.905  1.770 1.00 38.95   A2
ATOM  687 O   ALA  92   36.294 78.687  2.194 1.00 42.45   A2
ATOM  688 N   LEU  93   37.151 76.618  2.123 1.00 38.34   A2
ATOM  689 H   LEU  93   37.855 76.040  1.759 1.00  0.00   A2
ATOM  690 CA  LEU  93   36.111 76.018  2.972 1.00 36.90   A2
ATOM  691 CB  LEU  93   36.088 74.463  2.794 1.00 35.34   A2
ATOM  692 CG  LEU  93   35.725 73.992  1.378 1.00 33.55   A2
ATOM  693 CD1 LEU  93   36.159 72.583  1.129 1.00 33.26   A2
ATOM  694 CD2 LEU  93   34.254 74.167  1.215 1.00 32.18   A2
ATOM  695 C   LEU  93   36.264 76.353  4.426 1.00 36.44   A2
ATOM  696 O   LEU  93   35.473 75.917  5.256 1.00 35.17   A2
ATOM  697 N   GLU  94   37.357 77.019  4.736 1.00 38.19   A2
ATOM  698 H   GLU  94   38.022 77.167  4.035 1.00  0.00   A2
ATOM  699 CA  GLU  94   37.627 77.573  6.038 1.00 42.71   A2
ATOM  700 CB  GLU  94   36.931 78.947  6.165 1.00 47.38   A2
ATOM  701 CG  GLU  94   37.418 80.011  5.131 1.00 56.10   A2
ATOM  702 CD  GLU  94   36.423 81.153  4.862 1.00 60.26   A2
ATOM  703 OE1 GLU  94   35.728 81.109  3.823 1.00 60.76   A2
ATOM  704 OE2 GLU  94   36.331 82.054  5.721 1.00 61.64   A2
ATOM  705 C   GLU  94   37.245 76.701  7.198 1.00 43.90   A2
ATOM  706 O   GLU  94   36.624 77.172  8.167 1.00 45.70   A2
ATOM  707 N   GLY  95   37.641 75.410  7.001 1.00 44.03   A2
ATOM  708 H   GLY  95   38.024 75.192  6.127 1.00  0.00   A2
ATOM  709 CA  GLY  95   37.519 74.310  7.981 1.00 42.49   A2
ATOM  710 C   GLY  95   36.162 73.612  8.061 1.00 42.24   A2
ATOM  711 O   GLY  95   36.028 72.596  8.739 1.00 40.02   A2
ATOM  712 N   ILE  96   35.160 74.123  7.328 1.00 42.82   A2
ATOM  713 H   ILE  96   35.357 74.944  6.841 1.00  0.00   A2
ATOM  714 CA  ILE  96   33.760 73.692  7.312 1.00 42.12   A2
ATOM  715 CB  ILE  96   33.665 72.233  6.800 1.00 36.33   A2
ATOM  716 CG2 ILE  96   32.248 71.768  6.789 1.00 34.79   A2
ATOM  717 CG1 ILE  96   34.091 72.157  5.374 1.00 35.35   A2
ATOM  718 CD  ILE  96   34.051 70.743  4.738 1.00 33.64   A2
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FIG.5K

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ATOM  719 C  ILE  96   33.106 73.863  8.709 1.00 44.74   A2
ATOM  720 O  ILE  96   32.220 74.716  8.841 1.00 44.59   A2
ATOM  721 N  SER  97   33.467 73.154  9.780 1.00 46.84   A2
ATOM  722 H  SER  97   34.243 72.553  9.706 1.00  0.00   A2
ATOM  723 CA SER  97   32.900 73.359 11.105 1.00 48.91   A2
ATOM  724 CB SER  97   31.804 72.343 11.347 1.00 49.60   A2
ATOM  725 OG SER  97   32.211 71.120 11.954 1.00 52.85   A2
ATOM  726 HG SER  97   31.406 70.573 11.942 1.00  0.00   A2
ATOM  727 C  SER  97   34.045 73.143 12.077 1.00 50.64   A2
ATOM  728 O  SER  97   35.035 72.538 11.678 1.00 52.78   A2
ATOM  729 N  PRO  98   34.063 73.474 13.348 1.00 52.12   A2
ATOM  730 CD PRO  98   33.002 74.170 14.016 1.00 52.90   A2
ATOM  731 CA PRO  98   35.195 73.200 14.257 1.00 54.94   A2
ATOM  732 CB PRO  98   34.750 73.717 15.600 1.00 54.78   A2
ATOM  733 CG PRO  98   33.772 74.777 15.182 1.00 55.48   A2
ATOM  734 C  PRO  98   35.591 71.723 14.336 1.00 56.75   A2
ATOM  735 O  PRO  98   36.738 71.274 14.468 1.00 57.85   A2
ATOM  736 N  GLU  99   34.509 70.971 14.214 1.00 58.21   A2
ATOM  737 H  GLU  99   33.652 71.400 14.028 1.00  0.00   A2
ATOM  738 CA GLU  99   34.543 69.537 14.281 1.00 58.48   A2
ATOM  739 CB GLU  99   33.111 69.104 14.304 1.00 63.30   A2
ATOM  740 CG GLU  99   32.958 67.702 14.852 1.00 71.04   A2
ATOM  741 CD GLU  99   32.076 66.838 13.962 1.00 76.95   A2
ATOM  742 OE1 GLU  99   32.209 65.608 14.079 1.00 80.63   A2
ATOM  743 OE2 GLU  99   31.295 67.382 13.153 1.00 77.99   A2
ATOM  744 C  GLU  99   35.298 69.025 13.074 1.00 55.31   A2
ATOM  745 O  GLU  99   36.251 68.270 13.210 1.00 55.96   A2
ATOM  746 N  LEU 100   34.916 69.475 11.891 1.00 51.23   A2
ATOM  747 H  LEU 100   34.214 70.159 11.841 1.00  0.00   A2
ATOM  748 CA LEU 100   35.577 69.052 10.678 1.00 48.08   A2
ATOM  749 CB LEU 100   34.627 69.341  9.574 1.00 45.52   A2
ATOM  750 CG LEU 100   33.544 68.337  9.674 1.00 45.39   A2
ATOM  751 CD1 LEU 100   32.207 68.972  9.458 1.00 46.40   A2
ATOM  752 CD2 LEU 100   33.851 67.245  8.677 1.00 47.48   A2
ATOM  753 C  LEU 100   36.956 69.629 10.368 1.00 46.77   A2
ATOM  754 O  LEU 100   37.578 69.244  9.357 1.00 46.62   A2
ATOM  755 N  GLY 101   37.441 70.505 11.272 1.00 45.40   A2
ATOM  756 H  GLY 101   36.893 70.704 12.056 1.00  0.00   A2
ATOM  757 CA GLY 101   38.703 71.238 11.126 1.00 42.52   A2
ATOM  758 C  GLY 101   39.885 70.334 10.798 1.00 40.73   A2
ATOM  759 O  GLY 101   40.475 70.402  9.710 1.00 40.69   A2
ATOM  760 N  PRO 102   40.250 69.441 11.708 1.00 38.61   A2
ATOM  761 CD PRO 102   39.676 69.350 13.027 1.00 39.26   A2
ATOM  762 CA PRO 102   41.390 68.566 11.606 1.00 37.30   A2
ATOM  763 CB PRO 102   41.294 67.690 12.775 1.00 39.36   A2
ATOM  764 CG PRO 102   40.799 68.687 13.776 1.00 41.02   A2
ATOM  765 C  PRO 102   41.364 67.795 10.331 1.00 37.15   A2
ATOM  766 O  PRO 102   42.358 67.854  9.600 1.00 38.88   A2
ATOM  767 N  THR 103   40.223 67.167 10.045 1.00 35.36   A2
ATOM  768 H  THR 103   39.466 67.223 10.662 1.00  0.00   A2
ATOM  769 CA THR 103   40.051 66.386  8.843 1.00 34.62   A2
ATOM  770 CB THR 103   38.592 65.888  8.715 1.00 34.07   A2
ATOM  771 OG1 THR 103   38.356 65.240  9.936 1.00 35.43   A2
ATOM  772 HG1 THR 103   38.011 65.896 10.548 1.00  0.00   A2
ATOM  773 CG2 THR 103   38.312 64.896  7.594 1.00 31.29   A2
ATOM  774 C  THR 103   40.417 67.215  7.625 1.00 34.61   A2
ATOM  775 O  THR 103   41.091 66.665  6.738 1.00 38.16   A2
ATOM  776 N  LEU 104   40.054 68.498  7.529 1.00 32.49   A2
ATOM  777 H  LEU 104   39.504 68.923  8.229 1.00  0.00   A2
ATOM  778 CA LEU 104   40.471 69.267  6.370 1.00 30.49   A2
ATOM  779 CB LEU 104   39.616 70.430  6.242 1.00 33.51   A2
ATOM  780 CG LEU 104   38.356 69.996  5.611 1.00 36.61   A2
ATOM  781 CD1 LEU 104   37.222 70.621  6.381 1.00 39.43   A2
ATOM  782 CD2 LEU 104   38.418 70.294  4.132 1.00 37.89   A2
ATOM  783 C  LEU 104   41.904 69.727  6.414 1.00 28.48   A2
ATOM  784 O  LEU 104   42.583 69.825  5.398 1.00 28.47   A2
ATOM  785 N  ASP 105   42.449 69.949  7.574 1.00 26.99   A2
ATOM  786 H  ASP 105   41.903 69.912  8.388 1.00  0.00   A2
ATOM  787 CA ASP 105   43.822 70.307  7.613 1.00 28.67   A2
ATOM  788 CB ASP 105   44.139 70.584  9.038 1.00 33.06   A2
ATOM  789 CG ASP 105   43.438 71.808  9.593 1.00 35.46   A2
ATOM  790 OD1 ASP 105   43.085 72.726  8.836 1.00 38.42   A2
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FIG.5L

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ATOM  791 OD2 ASP 105    43.244 71.816 10.808 1.00 39.10    A2
ATOM  792 C  ASP 105    44.701 69.206  7.032 1.00 28.90    A2
ATOM  793 O  ASP 105    45.551 69.479  6.175 1.00 29.62    A2
ATOM  794 N  THR 106    44.415 67.950  7.401 1.00 26.86    A2
ATOM  795 H  THR 106    43.674 67.826  8.029 1.00  0.00    A2
ATOM  796 CA THR 106    45.143 66.770  6.935 1.00 24.81    A2
ATOM  797 CB THR 106    44.558 65.456  7.477 1.00 26.03    A2
ATOM  798 OG1 THR 106    44.680 65.566  8.894 1.00 31.53    A2
ATOM  799 HG1 THR 106    44.069 66.223  9.242 1.00  0.00    A2
ATOM  800 CG2 THR 106    45.258 64.220  7.011 1.00 20.90    A2
ATOM  801 C  THR 106    45.073 66.684  5.460 1.00 23.75    A2
ATOM  802 O  THR 106    46.065 66.411  4.812 1.00 24.68    A2
ATOM  803 N  LEU 107    43.887 66.917  4.946 1.00 24.30    A2
ATOM  804 H  LEU 107    43.145 67.176  5.528 1.00  0.00    A2
ATOM  805 CA LEU 107    43.668 66.783  3.531 1.00 27.29    A2
ATOM  806 CB LEU 107    42.158 66.913  3.273 1.00 25.45    A2
ATOM  807 CG LEU 107    41.642 66.888  1.863 1.00 26.24    A2
ATOM  808 CD1 LEU 107    42.095 65.649  1.158 1.00 26.41    A2
ATOM  809 CD2 LEU 107    40.140 66.925  1.914 1.00 27.62    A2
ATOM  810 C  LEU 107    44.485 67.848  2.819 1.00 28.01    A2
ATOM  811 O  LEU 107    45.154 67.555  1.823 1.00 30.72    A2
ATOM  812 N  GLN 108    44.540 69.055  3.373 1.00 28.52    A2
ATOM  813 H  GLN 108    44.030 69.221  4.194 1.00  0.00    A2
ATOM  814 CA GLN 108    45.343 70.132  2.792 1.00 28.38    A2
ATOM  815 CB GLN 108    45.138 71.363  3.630 1.00 30.15    A2
ATOM  816 CG GLN 108    43.711 71.787  3.542 1.00 32.67    A2
ATOM  817 CD GLN 108    43.606 73.192  4.048 1.00 35.24    A2
ATOM  818 OE1 GLN 108    43.085 73.484  5.125 1.00 36.07    A2
ATOM  819 NE2 GLN 108    44.189 74.044  3.213 1.00 33.58    A2
ATOM  820 HE21 GLN 108    44.582 73.701  2.386 1.00  0.00    A2
ATOM  821 HE22 GLN 108    44.195 74.986  3.471 1.00  0.00    A2
ATOM  822 C  GLN 108    46.840 69.842  2.675 1.00 26.40    A2
ATOM  823 O  GLN 108    47.450 69.955  1.597 1.00 27.57    A2
ATOM  824 N  LEU 109    47.388 69.473  3.833 1.00 25.81    A2
ATOM  825 H  LEU 109    46.795 69.495  4.615 1.00  0.00    A2
ATOM  826 CA LEU 109    48.764 69.003  4.043 1.00 27.96    A2
ATOM  827 CB LEU 109    48.951 68.637  5.513 1.00 29.41    A2
ATOM  828 CG LEU 109    48.712 69.771  6.520 1.00 31.78    A2
ATOM  829 CD1 LEU 109    48.750 69.188  7.933 1.00 29.16    A2
ATOM  830 CD2 LEU 109    49.724 70.889  6.285 1.00 32.19    A2
ATOM  831 C  LEU 109    49.168 67.790  3.186 1.00 26.80    A2
ATOM  832 O  LEU 109    50.214 67.721  2.544 1.00 26.81    A2
ATOM  833 N  ASP 110    48.305 66.807  3.090 1.00 25.98    A2
ATOM  834 H  ASP 110    47.471 66.835  3.600 1.00  0.00    A2
ATOM  835 CA ASP 110    48.590 65.684  2.250 1.00 23.32    A2
ATOM  836 CB ASP 110    47.577 64.570  2.553 1.00 26.34    A2
ATOM  837 CG ASP 110    47.905 63.878  3.894 1.00 31.10    A2
ATOM  838 OD1 ASP 110    47.070 63.093  4.323 1.00 34.98    A2
ATOM  839 OD2 ASP 110    48.958 64.107  4.535 1.00 34.06    A2
ATOM  840 C  ASP 110    48.557 66.138  0.842 1.00 21.31    A2
ATOM  841 O  ASP 110    49.493 65.711  0.165 1.00 20.63    A2
ATOM  842 N  VAL 111    47.627 66.998  0.363 1.00 20.80    A2
ATOM  843 H  VAL 111    46.900 67.310  0.944 1.00  0.00    A2
ATOM  844 CA VAL 111    47.711 67.454 -1.019 1.00 20.44    A2
ATOM  845 CB VAL 111    46.531 68.364 -1.376 1.00 23.60    A2
ATOM  846 CG1 VAL 111    46.615 68.946 -2.808 1.00 23.04    A2
ATOM  847 CG2 VAL 111    45.289 67.497 -1.371 1.00 24.30    A2
ATOM  848 C  VAL 111    49.006 68.224 -1.245 1.00 20.82    A2
ATOM  849 O  VAL 111    49.617 68.006 -2.303 1.00 19.22    A2
ATOM  850 N  ALA 112    49.442 69.063 -0.267 1.00 21.84    A2
ATOM  851 H  ALA 112    48.839 69.190  0.492 1.00  0.00    A2
ATOM  852 CA ALA 112    50.708 69.805 -0.295 1.00 24.16    A2
ATOM  853 CB ALA 112    50.861 70.561  1.011 1.00 22.69    A2
ATOM  854 C  ALA 112    51.931 68.878 -0.486 1.00 28.58    A2
ATOM  855 O  ALA 112    52.778 69.026 -1.390 1.00 32.53    A2
ATOM  856 N  ASP 113    52.086 67.852  0.343 1.00 30.21    A2
ATOM  857 H  ASP 113    51.507 67.817  1.130 1.00  0.00    A2
ATOM  858 CA ASP 113    53.084 66.846  0.166 1.00 31.70    A2
ATOM  859 CB ASP 113    52.706 65.659  0.953 1.00 36.31    A2
ATOM  860 CG ASP 113    53.170 65.758  2.357 1.00 42.27    A2
ATOM  861 OD1 ASP 113    52.559 65.109  3.203 1.00 46.37    A2
ATOM  862 OD2 ASP 113    54.160 66.461  2.589 1.00 48.93    A2
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FIG.5M

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ATOM  863 C   ASP 113   53.315 66.361 -1.239 1.00 32.82   A2
ATOM  864 O   ASP 113   54.433 66.308 -1.754 1.00 36.25   A2
ATOM  865 N   PHE 114   52.187 65.978 -1.830 1.00 30.94   A2
ATOM  866 H   PHE 114   51.344 66.164 -1.361 1.00  0.00   A2
ATOM  867 CA  PHE 114   52.109 65.328 -3.103 1.00 27.84   A2
ATOM  868 CB  PHE 114   50.708 64.794 -3.226 1.00 23.18   A2
ATOM  869 CG  PHE 114   50.565 63.928 -4.420 1.00 21.04   A2
ATOM  870 CD1 PHE 114   51.623 63.225 -4.938 1.00 24.05   A2
ATOM  871 CD2 PHE 114   49.369 63.914 -5.046 1.00 22.37   A2
ATOM  872 CE1 PHE 114   51.476 62.514 -6.102 1.00 24.54   A2
ATOM  873 CE2 PHE 114   49.211 63.207 -6.212 1.00 21.33   A2
ATOM  874 CZ  PHE 114   50.263 62.509 -6.741 1.00 24.71   A2
ATOM  875 C   PHE 114   52.453 66.291 -4.190 1.00 29.20   A2
ATOM  876 O   PHE 114   53.072 65.883 -5.158 1.00 30.84   A2
ATOM  877 N   ALA 115   52.057 67.554 -4.058 1.00 31.99   A2
ATOM  878 H   ALA 115   51.446 67.768 -3.317 1.00  0.00   A2
ATOM  879 CA  ALA 115   52.423 68.655 -4.952 1.00 31.29   A2
ATOM  880 CB  ALA 115   51.824 69.939 -4.420 1.00 30.65   A2
ATOM  881 C   ALA 115   53.936 68.787 -4.976 1.00 31.31   A2
ATOM  882 O   ALA 115   54.539 68.823 -6.044 1.00 30.36   A2
ATOM  883 N   THR 116   54.551 68.846 -3.813 1.00 32.20   A2
ATOM  884 H   THR 116   54.013 68.910 -2.992 1.00  0.00   A2
ATOM  885 CA  THR 116   55.998 68.897 -3.656 1.00 34.91   A2
ATOM  886 CB  THR 116   56.325 68.953 -2.150 1.00 35.78   A2
ATOM  887 OG1 THR 116   55.564 70.038 -1.576 1.00 35.58   A2
ATOM  888 HG1 THR 116   54.942 69.644 -0.939 1.00  0.00   A2
ATOM  889 CG2 THR 116   57.816 69.050 -1.921 1.00 35.38   A2
ATOM  890 C   THR 116   56.714 67.726 -4.304 1.00 37.14   A2
ATOM  891 O   THR 116   57.641 67.937 -5.066 1.00 39.27   A2
ATOM  892 N   THR 117   56.318 66.485 -4.045 1.00 39.05   A2
ATOM  893 H   THR 117   55.615 66.383 -3.369 1.00  0.00   A2
ATOM  894 CA  THR 117   56.840 65.269 -4.630 1.00 40.23   A2
ATOM  895 CB  THR 117   55.909 64.090 -4.216 1.00 39.99   A2
ATOM  896 OG1 THR 117   56.149 63.920 -2.820 1.00 41.66   A2
ATOM  897 HG1 THR 117   55.653 64.559 -2.286 1.00  0.00   A2
ATOM  898 CG2 THR 117   56.110 62.781 -4.981 1.00 38.23   A2
ATOM  899 C   THR 117   56.882 65.417 -6.134 1.00 43.42   A2
ATOM  900 O   THR 117   57.934 65.253 -6.749 1.00 46.29   A2
ATOM  901 N   ILE 118   55.763 65.777 -6.741 1.00 45.87   A2
ATOM  902 H   ILE 118   54.962 65.942 -6.200 1.00  0.00   A2
ATOM  903 CA  ILE 118   55.659 65.914 -8.182 1.00 47.97   A2
ATOM  904 CB  ILE 118   54.170 66.271 -8.452 1.00 47.69   A2
ATOM  905 CG2 ILE 118   54.041 66.930 -9.835 1.00 47.03   A2
ATOM  906 CG1 ILE 118   53.302 65.011 -8.244 1.00 44.00   A2
ATOM  907 CD  ILE 118   53.651 63.883 -9.236 1.00 43.71   A2
ATOM  908 C   ILE 118   56.647 66.932 -8.724 1.00 50.69   A2
ATOM  909 O   ILE 118   57.390 66.676 -9.681 1.00 49.98   A2
ATOM  910 N   TRP 119   56.697 68.061 -8.015 1.00 54.68   A2
ATOM  911 H   TRP 119   56.164 68.135 -7.197 1.00  0.00   A2
ATOM  912 CA  TRP 119   57.575 69.142 -8.399 1.00 58.98   A2
ATOM  913 CB  TRP 119   57.392 70.367 -7.477 1.00 59.84   A2
ATOM  914 CG  TRP 119   58.051 71.529 -8.196 1.00 62.64   A2
ATOM  915 CD2 TRP 119   57.596 72.211 -9.307 1.00 63.78   A2
ATOM  916 CE2 TRP 119   58.699 72.955 -9.643 1.00 62.55   A2
ATOM  917 CE3 TRP 119   56.465 72.314 -10.080 1.00 66.02   A2
ATOM  918 CD1 TRP 119   59.322 71.870 -7.863 1.00 64.12   A2
ATOM  919 NE1 TRP 119   59.680 72.727 -8.784 1.00 65.00   A2
ATOM  920 HE1 TRP 119   60.568 73.140 -8.828 1.00  0.00   A2
ATOM  921 CZ2 TRP 119   58.726 73.794 -10.714 1.00 62.90   A2
ATOM  922 CZ3 TRP 119   56.469 73.157 -11.170 1.00 65.18   A2
ATOM  923 CH2 TRP 119   57.591 73.887 -11.481 1.00 64.40   A2
ATOM  924 C   TRP 119   59.021 68.664 -8.352 1.00 61.26   A2
ATOM  925 O   TRP 119   59.748 68.788 -9.343 1.00 62.12   A2
ATOM  926 N   GLN 120   59.447 68.065 -7.249 1.00 62.91   A2
ATOM  927 H   GLN 120   58.811 67.961 -6.519 1.00  0.00   A2
ATOM  928 CA  GLN 120   60.786 67.504 -7.113 1.00 65.16   A2
ATOM  929 CB  GLN 120   60.900 66.800 -5.780 1.00 66.56   A2
ATOM  930 CG  GLN 120   60.627 67.678 -4.582 1.00 67.18   A2
ATOM  931 CD  GLN 120   60.725 66.907 -3.284 1.00 67.77   A2
ATOM  932 OE1 GLN 120   61.221 67.465 -2.319 1.00 69.31   A2
ATOM  933 NE2 GLN 120   60.305 65.654 -3.129 1.00 67.39   A2
ATOM  934 HE21 GLN 120   59.903 65.174 -3.877 1.00  0.00   A2
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FIG.5N

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ATOM  935 HE22 GLN  120     60.441  65.282  -2.234  1.00  0.00      A2
ATOM  936  C   GLN  120     61.169  66.509  -8.222  1.00 66.22      A2
ATOM  937  O   GLN  120     62.326  66.421  -8.662  1.00 66.50      A2
ATOM  938  N   GLN  121     60.202  65.745  -8.706  1.00 67.10      A2
ATOM  939  H   GLN  121     59.307  65.754  -8.303  1.00  0.00      A2
ATOM  940  CA  GLN  121     60.480  64.878  -9.812  1.00 68.66      A2
ATOM  941  CB  GLN  121     59.292  63.971 -10.070  1.00 67.96      A2
ATOM  942  CG  GLN  121     59.614  62.937 -11.128  1.00 68.89      A2
ATOM  943  CD  GLN  121     60.940  62.236 -10.852  1.00 71.37      A2
ATOM  944  OE1 GLN  121     61.212  61.706  -9.777  1.00 71.70      A2
ATOM  945  NE2 GLN  121     61.879  62.262 -11.786  1.00 74.41      A2
ATOM  946 HE21 GLN  121     61.707  62.729 -12.627  1.00  0.00      A2
ATOM  947 HE22 GLN  121     62.736  61.859 -11.541  1.00  0.00      A2
ATOM  948  C   GLN  121     60.760  65.743 -11.045  1.00 70.48      A2
ATOM  949  O   GLN  121     61.671  65.436 -11.827  1.00 70.94      A2
ATOM  950  N   MET  122     60.019  66.846 -11.236  1.00 71.67      A2
ATOM  951  H   MET  122     59.351  67.087 -10.555  1.00  0.00      A2
ATOM  952  CA  MET  122     60.190  67.688 -12.412  1.00 72.62      A2
ATOM  953  CB  MET  122     59.173  68.819 -12.448  1.00 73.12      A2
ATOM  954  CG  MET  122     57.880  68.343 -13.083  1.00 73.64      A2
ATOM  955  SD  MET  122     56.669  69.662 -13.295  1.00 75.44      A2
ATOM  956  CE  MET  122     55.695  69.349 -11.861  1.00 76.43      A2
ATOM  957  C   MET  122     61.566  68.281 -12.411  1.00 73.22      A2
ATOM  958  O   MET  122     62.240  68.287 -13.441  1.00 73.03      A2
ATOM  959  N   GLU  123     61.991  68.697 -11.223  1.00 74.74      A2
ATOM  960  H   GLU  123     61.372  68.617 -10.466  1.00  0.00      A2
ATOM  961  CA  GLU  123     63.305  69.262 -11.018  1.00 75.95      A2
ATOM  962  CB  GLU  123     63.484  69.665  -9.597  1.00 75.72      A2
ATOM  963  CG  GLU  123     62.644  70.906  -9.500  1.00 79.11      A2
ATOM  964  CD  GLU  123     62.651  71.529  -8.122  1.00 83.02      A2
ATOM  965  OE1 GLU  123     62.741  72.763  -8.057  1.00 84.15      A2
ATOM  966  OE2 GLU  123     62.543  70.789  -7.133  1.00 84.45      A2
ATOM  967  C   GLU  123     64.381  68.280 -11.386  1.00 77.17      A2
ATOM  968  O   GLU  123     65.092  68.558 -12.356  1.00 78.22      A2
ATOM  969  N   GLU  124     64.504  67.110 -10.765  1.00 77.66      A2
ATOM  970  H   GLU  124     63.867  66.852 -10.060  1.00  0.00      A2
ATOM  971  CA  GLU  124     65.574  66.215 -11.167  1.00 78.47      A2
ATOM  972  CB  GLU  124     65.600  65.051 -10.195  1.00 80.79      A2
ATOM  973  CG  GLU  124     64.387  64.132 -10.150  1.00 83.29      A2
ATOM  974  CD  GLU  124     64.375  63.248  -8.908  1.00 85.51      A2
ATOM  975  OE1 GLU  124     64.733  63.729  -7.824  1.00 86.84      A2
ATOM  976  OE2 GLU  124     64.006  62.075  -9.024  1.00 86.39      A2
ATOM  977  C   GLU  124     65.534  65.705 -12.612  1.00 78.01      A2
ATOM  978  O   GLU  124     66.480  65.057 -13.060  1.00 78.91      A2
ATOM  979  N   LEU  125     64.460  65.943 -13.363  1.00 77.11      A2
ATOM  980  H   LEU  125     63.666  66.340 -12.945  1.00  0.00      A2
ATOM  981  CA  LEU  125     64.387  65.583 -14.771  1.00 76.23      A2
ATOM  982  CB  LEU  125     63.061  64.832 -14.952  1.00 76.88      A2
ATOM  983  CG  LEU  125     62.392  64.382 -16.263  1.00 76.63      A2
ATOM  984  CD1 LEU  125     63.350  63.754 -17.276  1.00 76.67      A2
ATOM  985  CD2 LEU  125     61.309  63.402 -15.839  1.00 75.89      A2
ATOM  986  C   LEU  125     64.506  66.827 -15.648  1.00 75.84      A2
ATOM  987  O   LEU  125     64.360  66.788 -16.871  1.00 75.36      A2
ATOM  988  N   GLY  126     64.759  67.968 -15.027  1.00 75.90      A2
ATOM  989  H   GLY  126     64.741  67.976 -14.056  1.00  0.00      A2
ATOM  990  CA  GLY  126     64.968  69.213 -15.736  1.00 77.58      A2
ATOM  991  C   GLY  126     63.697  69.814 -16.330  1.00 78.63      A2
ATOM  992  O   GLY  126     63.735  70.736 -17.146  1.00 78.55      A2
ATOM  993  N   MET  127     62.524  69.343 -15.933  1.00 80.08      A2
ATOM  994  H   MET  127     62.522  68.603 -15.293  1.00  0.00      A2
ATOM  995  CA  MET  127     61.266  69.902 -16.415  1.00 81.46      A2
ATOM  996  CB  MET  127     60.191  68.802 -16.361  1.00 81.86      A2
ATOM  997  CG  MET  127     60.708  67.599 -17.147  1.00 82.66      A2
ATOM  998  SD  MET  127     59.682  66.115 -17.282  1.00 83.70      A2
ATOM  999  CE  MET  127     60.236  65.620 -18.900  1.00 83.23      A2
ATOM 1000  C   MET  127     60.847  71.131 -15.599  1.00 82.18      A2
ATOM 1001 OT1 MET  127     60.116  71.958 -16.142  1.00 83.86      A2
ATOM 1002 OT2 MET  127     61.267  71.285 -14.446  1.00 82.04      A2
ATOM 1003  CB  MET  138     39.323  80.595  -4.492  1.00 59.39      A3
ATOM 1004  CG  MET  138     40.123  79.298  -4.421  1.00 57.97      A3
ATOM 1005  SD  MET  138     40.561  78.973  -6.145  1.00 60.85      A3
ATOM 1006  CE  MET  138     41.129  77.310  -6.351  1.00 61.48      A3
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FIG.50

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ATOM 1007 C  MET 138  37.021 81.072 -5.454 1.00 60.26  A3
ATOM 1008 O  MET 138  36.832 82.262 -5.181 1.00 62.98  A3
ATOM 1009 HT1 MET 138  38.497 82.600 -6.075 1.00 0.00  A3
ATOM 1010 HT2 MET 138  38.313 81.757 -7.529 1.00 0.00  A3
ATOM 1011 N  MET 138  38.839 81.784 -6.639 1.00 60.49  A3
ATOM 1012 HT3 MET 138  39.865 81.816 -6.768 1.00 0.00  A3
ATOM 1013 CA MET 138  38.445 80.672 -5.787 1.00 60.51  A3
ATOM 1014 N  PRO 139  35.995 80.242 -5.612 1.00 57.82  A3
ATOM 1015 CD PRO 139  36.028 79.060 -6.448 1.00 58.10  A3
ATOM 1016 CA PRO 139  34.654 80.538 -5.142 1.00 54.67  A3
ATOM 1017 CB PRO 139  33.870 79.323 -5.525 1.00 54.54  A3
ATOM 1018 CG PRO 139  34.945 78.290 -5.755 1.00 58.20  A3
ATOM 1019 C  PRO 139  34.588 80.875 -3.664 1.00 52.24  A3
ATOM 1020 O  PRO 139  35.507 80.623 -2.882 1.00 51.89  A3
ATOM 1021 N  ALA 140  33.499 81.547 -3.342 1.00 49.86  A3
ATOM 1022 H  ALA 140  32.789 81.676 -4.005 1.00 0.00  A3
ATOM 1023 CA ALA 140  33.234 81.926 -1.994 1.00 49.39  A3
ATOM 1024 CB ALA 140  32.966 83.413 -1.895 1.00 49.94  A3
ATOM 1025 C  ALA 140  31.978 81.153 -1.590 1.00 49.25  A3
ATOM 1026 O  ALA 140  30.889 81.162 -2.205 1.00 49.06  A3
ATOM 1027 N  PHE 141  32.293 80.442 -0.506 1.00 47.48  A3
ATOM 1028 H  PHE 141  33.190 80.550 -0.122 1.00 0.00  A3
ATOM 1029 CA PHE 141  31.401 79.552  0.208 1.00 45.66  A3
ATOM 1030 CB PHE 141  32.215 78.305  0.792 1.00 40.28  A3
ATOM 1031 CG PHE 141  32.684 77.404 -0.349 1.00 35.35  A3
ATOM 1032 CD1 PHE 141  31.800 76.591 -1.006 1.00 34.39  A3
ATOM 1033 CD2 PHE 141  33.966 77.497 -0.830 1.00 37.69  A3
ATOM 1034 CE1 PHE 141  32.174 75.895 -2.133 1.00 34.00  A3
ATOM 1035 CE2 PHE 141  34.358 76.807 -1.956 1.00 36.69  A3
ATOM 1036 CZ PHE 141  33.449 76.001 -2.614 1.00 37.29  A3
ATOM 1037 C  PHE 141  31.003 80.580  1.242 1.00 46.54  A3
ATOM 1038 O  PHE 141  31.584 80.664  2.317 1.00 48.26  A3
ATOM 1039 N  ALA 142  30.067 81.452  0.843 1.00 47.38  A3
ATOM 1040 H  ALA 142  29.624 81.295 -0.020 1.00 0.00  A3
ATOM 1041 CA ALA 142  29.581 82.564  1.668 1.00 46.06  A3
ATOM 1042 CB ALA 142  28.731 83.546  0.879 1.00 45.04  A3
ATOM 1043 C  ALA 142  28.703 82.132  2.802 1.00 45.27  A3
ATOM 1044 O  ALA 142  28.343 83.002  3.584 1.00 47.38  A3
ATOM 1045 N  SER 143  28.318 80.860  2.899 1.00 43.36  A3
ATOM 1046 H  SER 143  28.724 80.201  2.303 1.00 0.00  A3
ATOM 1047 CA SER 143  27.377 80.392  3.897 1.00 41.94  A3
ATOM 1048 CB SER 143  26.036 80.129  3.181 1.00 44.17  A3
ATOM 1049 OG SER 143  25.323 78.918  3.536 1.00 48.18  A3
ATOM 1050 HG SER 143  24.455 78.974  3.098 1.00 0.00  A3
ATOM 1051 C  SER 143  27.877 79.145  4.602 1.00 39.79  A3
ATOM 1052 O  SER 143  28.763 78.452  4.132 1.00 38.50  A3
ATOM 1053 N  ALA 144  27.218 78.775  5.683 1.00 39.10  A3
ATOM 1054 H  ALA 144  26.449 79.312  5.960 1.00 0.00  A3
ATOM 1055 CA ALA 144  27.566 77.586  6.411 1.00 39.22  A3
ATOM 1056 CB ALA 144  26.982 77.598  7.802 1.00 36.97  A3
ATOM 1057 C  ALA 144  26.964 76.420  5.627 1.00 41.58  A3
ATOM 1058 O  ALA 144  27.706 75.448  5.444 1.00 42.07  A3
ATOM 1059 N  PHE 145  25.719 76.407  5.076 1.00 40.77  A3
ATOM 1060 H  PHE 145  25.149 77.203  5.110 1.00 0.00  A3
ATOM 1061 CA PHE 145  25.307 75.234  4.312 1.00 39.31  A3
ATOM 1062 CB PHE 145  23.877 75.396  3.798 1.00 36.46  A3
ATOM 1063 CG PHE 145  23.477 74.452  2.641 1.00 31.91  A3
ATOM 1064 CD1 PHE 145  23.579 74.900  1.323 1.00 29.02  A3
ATOM 1065 CD2 PHE 145  23.013 73.185  2.916 1.00 29.40  A3
ATOM 1066 CE1 PHE 145  23.225 74.100  0.277 1.00 28.34  A3
ATOM 1067 CE2 PHE 145  22.661 72.389  1.858 1.00 28.80  A3
ATOM 1068 CZ PHE 145  22.764 72.831  0.549 1.00 30.58  A3
ATOM 1069 C  PHE 145  26.266 75.071  3.120 1.00 40.44  A3
ATOM 1070 O  PHE 145  26.556 73.938  2.697 1.00 40.55  A3
ATOM 1071 N  GLN 146  26.745 76.232  2.619 1.00 39.11  A3
ATOM 1072 H  GLN 146  26.437 77.073  3.015 1.00 0.00  A3
ATOM 1073 CA GLN 146  27.660 76.263  1.511 1.00 38.01  A3
ATOM 1074 CB GLN 146  27.907 77.644  1.054 1.00 38.92  A3
ATOM 1075 CG GLN 146  26.884 78.066  0.049 1.00 43.26  A3
ATOM 1076 CD GLN 146  27.171 79.440 -0.522 1.00 45.37  A3
ATOM 1077 OE1 GLN 146  27.851 80.253  0.083 1.00 47.57  A3
ATOM 1078 NE2 GLN 146  26.689 79.793 -1.692 1.00 47.50  A3
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FIG.5P

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ATOM  1079 HE21 GLN  146      26.149  79.149  -2.190  1.00  0.00      A3
ATOM  1080 HE22 GLN  146      26.913  80.690  -2.021  1.00  0.00      A3
ATOM  1081  C   GLN  146      29.005  75.670   1.836  1.00 37.25      A3
ATOM  1082  O   GLN  146      29.634  75.093   0.950  1.00 38.28      A3
ATOM  1083  N   ARG  147      29.511  75.775   3.054  1.00 36.37      A3
ATOM  1084  H   ARG  147      29.044  76.300   3.738  1.00  0.00      A3
ATOM  1085  CA  ARG  147      30.798  75.180   3.357  1.00 35.68      A3
ATOM  1086  CB  ARG  147      31.299  75.574   4.713  1.00 37.12      A3
ATOM  1087  CG  ARG  147      31.730  77.016   4.697  1.00 42.68      A3
ATOM  1088  CD  ARG  147      32.034  77.494   6.093  1.00 49.54      A3
ATOM  1089  NE  ARG  147      32.674  78.774   5.877  1.00 58.21      A3
ATOM  1090  HE  ARG  147      32.475  79.252   5.045  1.00  0.00      A3
ATOM  1091  CZ  ARG  147      33.519  79.373   6.742  1.00 62.77      A3
ATOM  1092  NH1 ARG  147      33.905  78.868   7.936  1.00 63.96      A3
ATOM  1093 HH11 ARG  147      34.545  79.379   8.510  1.00  0.00      A3
ATOM  1094 HH12 ARG  147      33.561  77.980   8.239  1.00  0.00      A3
ATOM  1095  NH2 ARG  147      33.960  80.584   6.403  1.00 64.80      A3
ATOM  1096 HH21 ARG  147      34.599  81.069   6.999  1.00  0.00      A3
ATOM  1097 HH22 ARG  147      33.665  80.996   5.541  1.00  0.00      A3
ATOM  1098  C   ARG  147      30.570  73.702   3.337  1.00 34.91      A3
ATOM  1099  O   ARG  147      31.233  73.050   2.539  1.00 34.56      A3
ATOM  1100  N   ALA  148      29.544  73.194   4.040  1.00 33.44      A3
ATOM  1101  H   ALA  148      28.926  73.818   4.482  1.00  0.00      A3
ATOM  1102  CA  ALA  148      29.358  71.754   4.172  1.00 33.92      A3
ATOM  1103  CB  ALA  148      28.217  71.426   5.163  1.00 32.85      A3
ATOM  1104  C   ALA  148      29.077  71.095   2.843  1.00 33.40      A3
ATOM  1105  O   ALA  148      29.765  70.141   2.457  1.00 34.31      A3
ATOM  1106  N   ALA  149      28.169  71.657   2.077  1.00 32.60      A3
ATOM  1107  H   ALA  149      27.662  72.424   2.411  1.00  0.00      A3
ATOM  1108  CA  ALA  149      27.890  71.134   0.757  1.00 32.70      A3
ATOM  1109  CB  ALA  149      26.595  71.774   0.299  1.00 31.91      A3
ATOM  1110  C   ALA  149      29.032  71.381  -0.258  1.00 33.75      A3
ATOM  1111  O   ALA  149      29.208  70.661  -1.264  1.00 34.49      A3
ATOM  1112  N   GLY  150      29.867  72.401  -0.052  1.00 33.58      A3
ATOM  1113  H   GLY  150      29.724  73.035   0.682  1.00  0.00      A3
ATOM  1114  CA  GLY  150      31.017  72.608  -0.913  1.00 31.79      A3
ATOM  1115  C   GLY  150      32.113  71.629  -0.478  1.00 31.39      A3
ATOM  1116  O   GLY  150      32.997  71.261  -1.265  1.00 31.77      A3
ATOM  1117  N   GLY  151      32.075  71.161   0.773  1.00 29.83      A3
ATOM  1118  H   GLY  151      31.412  71.524   1.394  1.00  0.00      A3
ATOM  1119  CA  GLY  151      33.018  70.166   1.243  1.00 32.16      A3
ATOM  1120  C   GLY  151      32.764  68.909   0.409  1.00 33.98      A3
ATOM  1121  O   GLY  151      33.664  68.501  -0.349  1.00 35.66      A3
ATOM  1122  N   VAL  152      31.486  68.418   0.451  1.00 31.87      A3
ATOM  1123  H   VAL  152      30.867  68.906   1.040  1.00  0.00      A3
ATOM  1124  CA  VAL  152      30.978  67.240  -0.275  1.00 29.61      A3
ATOM  1125  CB  VAL  152      29.419  67.145  -0.125  1.00 27.63      A3
ATOM  1126  CG1 VAL  152      28.883  66.035  -0.976  1.00 27.37      A3
ATOM  1127  CG2 VAL  152      29.002  66.786   1.279  1.00 24.74      A3
ATOM  1128  C   VAL  152      31.351  67.294  -1.762  1.00 29.91      A3
ATOM  1129  O   VAL  152      31.805  66.329  -2.393  1.00 31.75      A3
ATOM  1130  N   LEU  153      31.236  68.452  -2.361  1.00 29.26      A3
ATOM  1131  H   LEU  153      30.881  69.219  -1.860  1.00  0.00      A3
ATOM  1132  CA  LEU  153      31.559  68.607  -3.756  1.00 26.77      A3
ATOM  1133  CB  LEU  153      30.881  69.858  -4.160  1.00 28.22      A3
ATOM  1134  CG  LEU  153      29.943  69.894  -5.316  1.00 30.67      A3
ATOM  1135  CD1 LEU  153      28.580  69.281  -5.090  1.00 26.48      A3
ATOM  1136  CD2 LEU  153      29.741  71.365  -5.496  1.00 34.46      A3
ATOM  1137  C   LEU  153      33.032  68.628  -4.111  1.00 26.08      A3
ATOM  1138  O   LEU  153      33.419  68.187  -5.212  1.00 26.78      A3
ATOM  1139  N   VAL  154      33.902  69.180  -3.269  1.00 26.12      A3
ATOM  1140  H   VAL  154      33.589  69.557  -2.416  1.00  0.00      A3
ATOM  1141  CA  VAL  154      35.330  69.259  -3.611  1.00 26.23      A3
ATOM  1142  CB  VAL  154      36.057  70.299  -2.692  1.00 26.51      A3
ATOM  1143  CG1 VAL  154      37.578  70.188  -2.942  1.00 25.01      A3
ATOM  1144  CG2 VAL  154      35.528  71.728  -2.945  1.00 27.82      A3
ATOM  1145  C   VAL  154      35.933  67.850  -3.375  1.00 26.80      A3
ATOM  1146  O   VAL  154      36.678  67.363  -4.229  1.00 26.27      A3
ATOM  1147  N   ALA  155      35.635  67.241  -2.199  1.00 24.76      A3
ATOM  1148  H   ALA  155      35.084  67.758  -1.570  1.00  0.00      A3
ATOM  1149  CA  ALA  155      36.095  65.940  -1.782  1.00 25.21      A3
ATOM  1150  CB  ALA  155      35.463  65.572  -0.457  1.00 25.25      A3
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FIG.5Q

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ATOM 1151 C  ALA 155   35.708 64.946 -2.841 1.00 26.94   A3
ATOM 1152 O  ALA 155   36.594 64.288 -3.398 1.00 26.76   A3
ATOM 1153 N  SER 156   34.450 64.982 -3.282 1.00 29.96   A3
ATOM 1154 H  SER 156   33.790 65.577 -2.868 1.00  0.00   A3
ATOM 1155 CA SER 156   34.034 64.105 -4.354 1.00 32.17   A3
ATOM 1156 CB SER 156   32.531 64.319 -4.544 1.00 34.23   A3
ATOM 1157 OG SER 156   32.000 64.195 -5.879 1.00 39.35   A3
ATOM 1158 HG SER 156   31.120 63.815 -5.851 1.00  0.00   A3
ATOM 1159 C  SER 156   34.845 64.338 -5.632 1.00 33.46   A3
ATOM 1160 O  SER 156   35.411 63.380 -6.174 1.00 34.62   A3
ATOM 1161 N  HIS 157   35.054 65.576 -6.133 1.00 33.90   A3
ATOM 1162 H  HIS 157   34.771 66.349 -5.605 1.00  0.00   A3
ATOM 1163 CA HIS 157   35.821 65.773 -7.383 1.00 31.19   A3
ATOM 1164 CB HIS 157   35.707 67.209 -7.900 1.00 32.59   A3
ATOM 1165 CG HIS 157   34.369 67.449 -8.566 1.00 31.11   A3
ATOM 1166 CD2 HIS 157  34.127 67.394 -9.928 1.00 30.78   A3
ATOM 1167 ND1 HIS 157  33.223 67.666 -7.942 1.00 32.36   A3
ATOM 1168 HD1 HIS 157  33.080 67.773 -6.979 1.00  0.00   A3
ATOM 1169 CE1 HIS 157  32.293 67.732 -8.875 1.00 32.01   A3
ATOM 1170 NE2 HIS 157  32.838 67.571 -10.060 1.00 29.18  A3
ATOM 1171 HE2 HIS 157  32.327 67.621 -10.895 1.00  0.00   A3
ATOM 1172 C  HIS 157   37.291 65.476 -7.269 1.00 29.68   A3
ATOM 1173 O  HIS 157   37.950 65.059 -8.219 1.00 29.65   A3
ATOM 1174 N  LEU 158   37.801 65.669 -6.071 1.00 29.24   A3
ATOM 1175 H  LEU 158   37.213 65.901 -5.326 1.00  0.00   A3
ATOM 1176 CA LEU 158   39.216 65.479 -5.826 1.00 31.94   A3
ATOM 1177 CB LEU 158   39.609 65.949 -4.373 1.00 28.66   A3
ATOM 1178 CG LEU 158   41.008 65.751 -3.859 1.00 24.32   A3
ATOM 1179 CD1 LEU 158  41.990 66.378 -4.776 1.00 20.87   A3
ATOM 1180 CD2 LEU 158  41.099 66.330 -2.477 1.00 24.86   A3
ATOM 1181 C  LEU 158   39.468 63.994 -6.027 1.00 31.46   A3
ATOM 1182 O  LEU 158   40.298 63.609 -6.844 1.00 30.58   A3
ATOM 1183 N  GLN 159   38.652 63.225 -5.340 1.00 33.54   A3
ATOM 1184 H  GLN 159   38.011 63.676 -4.748 1.00  0.00   A3
ATOM 1185 CA GLN 159   38.594 61.792 -5.442 1.00 35.73   A3
ATOM 1186 CB GLN 159   37.308 61.492 -4.813 1.00 37.26   A3
ATOM 1187 CG GLN 159   37.064 60.063 -4.520 1.00 45.01   A3
ATOM 1188 CD GLN 159   37.755 59.611 -3.256 1.00 46.24   A3
ATOM 1189 OE1 GLN 159  38.142 58.443 -3.232 1.00 48.29   A3
ATOM 1190 NE2 GLN 159  37.936 60.456 -2.224 1.00 47.82   A3
ATOM 1191 HE21 GLN 159 37.575 61.364 -2.289 1.00  0.00   A3
ATOM 1192 HE22 GLN 159 38.412 60.101 -1.447 1.00  0.00   A3
ATOM 1193 C  GLN 159   38.686 61.381 -6.921 1.00 36.24   A3
ATOM 1194 O  GLN 159   39.632 60.690 -7.324 1.00 38.97   A3
ATOM 1195 N  SER 160   37.824 61.896 -7.796 1.00 35.48   A3
ATOM 1196 H  SER 160   37.142 62.540 -7.498 1.00  0.00   A3
ATOM 1197 CA SER 160   37.869 61.564 -9.203 1.00 34.96   A3
ATOM 1198 CB SER 160   36.645 62.100 -9.863 1.00 37.54   A3
ATOM 1199 OG SER 160   35.587 62.434 -8.942 1.00 44.81   A3
ATOM 1200 HG SER 160   35.340 61.689 -8.387 1.00  0.00   A3
ATOM 1201 C  SER 160   39.090 62.095 -9.922 1.00 34.65   A3
ATOM 1202 O  SER 160   39.605 61.382 -10.785 1.00 35.42  A3
ATOM 1203 N  PHE 161   39.615 63.293 -9.595 1.00 33.82   A3
ATOM 1204 H  PHE 161   39.203 63.796 -8.864 1.00  0.00   A3
ATOM 1205 CA PHE 161   40.820 63.850 -10.218 1.00 31.21  A3
ATOM 1206 CB PHE 161   41.110 65.264 -9.629 1.00 28.28   A3
ATOM 1207 CG PHE 161   42.455 65.881 -10.062 1.00 24.92  A3
ATOM 1208 CD1 PHE 161  42.696 66.228 -11.389 1.00 22.98  A3
ATOM 1209 CD2 PHE 161  43.464 66.021 -9.135 1.00 23.03   A3
ATOM 1210 CE1 PHE 161  43.941 66.695 -11.767 1.00 21.06  A3
ATOM 1211 CE2 PHE 161  44.701 66.495 -9.528 1.00 20.28   A3
ATOM 1212 CZ PHE 161   44.939 66.826 -10.832 1.00 17.03  A3
ATOM 1213 C  PHE 161   42.008 62.907 -9.943 1.00 31.77   A3
ATOM 1214 O  PHE 161   42.786 62.578 -10.845 1.00 32.63  A3
ATOM 1215 N  LEU 162   42.117 62.434 -8.690 1.00 31.67   A3
ATOM 1216 H  LEU 162   41.420 62.691 -8.054 1.00  0.00   A3
ATOM 1217 CA LEU 162   43.186 61.574 -8.232 1.00 31.29   A3
ATOM 1218 CB LEU 162   43.204 61.433 -6.743 1.00 25.84   A3
ATOM 1219 CG LEU 162   43.693 62.674 -6.003 1.00 26.02   A3
ATOM 1220 CD1 LEU 162  43.594 62.455 -4.516 1.00 25.24   A3
ATOM 1221 CD2 LEU 162  45.107 62.994 -6.415 1.00 27.04   A3
ATOM 1222 C  LEU 162   43.061 60.212 -8.813 1.00 34.23   A3
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FIG.5R

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ATOM  1223  O   LEU  162     44.107  59.654  -9.070  1.00 36.51      A3
ATOM  1224  N   GLU  163     41.926  59.589  -9.082  1.00 37.24      A3
ATOM  1225  H   GLU  163     41.072  60.002  -8.826  1.00  0.00      A3
ATOM  1226  CA  GLU  163     41.975  58.327  -9.771  1.00 40.47      A3
ATOM  1227  CB  GLU  163     40.566  57.716  -9.835  1.00 45.38      A3
ATOM  1228  CG  GLU  163     40.264  56.975  -8.526  1.00 51.84      A3
ATOM  1229  CD  GLU  163     41.291  55.889  -8.126  1.00 57.97      A3
ATOM  1230  OE1 GLU  163     40.897  54.722  -8.092  1.00 62.01      A3
ATOM  1231  OE2 GLU  163     42.466  56.180  -7.832  1.00 59.17      A3
ATOM  1232  C   GLU  163     42.586  58.430 -11.142  1.00 41.34      A3
ATOM  1233  O   GLU  163     43.456  57.633 -11.486  1.00 42.17      A3
ATOM  1234  N   VAL  164     42.257  59.436 -11.920  1.00 42.28      A3
ATOM  1235  H   VAL  164     41.589  60.091 -11.615  1.00  0.00      A3
ATOM  1236  CA  VAL  164     42.911  59.609 -13.187  1.00 44.13      A3
ATOM  1237  CB  VAL  164     42.207  60.711 -13.940  1.00 45.52      A3
ATOM  1238  CG1 VAL  164     42.892  60.975 -15.278  1.00 48.79      A3
ATOM  1239  CG2 VAL  164     40.786  60.269 -14.226  1.00 46.09      A3
ATOM  1240  C   VAL  164     44.386  59.933 -12.991  1.00 46.13      A3
ATOM  1241  O   VAL  164     45.192  59.473 -13.794  1.00 45.99      A3
ATOM  1242  N   SER  165     44.879  60.677 -12.006  1.00 49.51      A3
ATOM  1243  H   SER  165     44.287  61.173 -11.396  1.00  0.00      A3
ATOM  1244  CA  SER  165     46.325  60.845 -11.895  1.00 53.44      A3
ATOM  1245  CB  SER  165     46.715  61.796 -10.775  1.00 54.77      A3
ATOM  1246  OG  SER  165     46.049  61.618  -9.530  1.00 59.99      A3
ATOM  1247  HG  SER  165     45.997  60.694  -9.261  1.00  0.00      A3
ATOM  1248  C   SER  165     46.958  59.502 -11.630  1.00 55.15      A3
ATOM  1249  O   SER  165     48.028  59.227 -12.148  1.00 55.02      A3
ATOM  1250  N   TYR  166     46.239  58.645 -10.900  1.00 58.57      A3
ATOM  1251  H   TYR  166     45.374  58.948 -10.549  1.00  0.00      A3
ATOM  1252  CA  TYR  166     46.617  57.273 -10.625  1.00 61.42      A3
ATOM  1253  CB  TYR  166     45.543  56.653  -9.680  1.00 64.05      A3
ATOM  1254  CG  TYR  166     45.502  55.138  -9.682  1.00 69.00      A3
ATOM  1255  CD1 TYR  166     44.389  54.501 -10.185  1.00 71.64      A3
ATOM  1256  CE1 TYR  166     44.367  53.130 -10.283  1.00 73.15      A3
ATOM  1257  CD2 TYR  166     46.594  54.409  -9.257  1.00 71.27      A3
ATOM  1258  CE2 TYR  166     46.584  53.040  -9.346  1.00 72.92      A3
ATOM  1259  CZ  TYR  166     45.468  52.417  -9.862  1.00 75.71      A3
ATOM  1260  OH  TYR  166     45.474  51.038 -10.016  1.00 80.61      A3
ATOM  1261  HH  TYR  166     44.571  50.736 -10.134  1.00  0.00      A3
ATOM  1262  C   TYR  166     46.712  56.567 -11.987  1.00 62.34      A3
ATOM  1263  O   TYR  166     47.766  55.981 -12.282  1.00 63.25      A3
ATOM  1264  N   ALA  167     45.727  56.622 -12.884  1.00 61.27      A3
ATOM  1265  H   ALA  167     44.893  57.089 -12.678  1.00  0.00      A3
ATOM  1266  CA  ALA  167     45.933  55.982 -14.159  1.00 61.47      A3
ATOM  1267  CB  ALA  167     44.608  55.904 -14.904  1.00 60.98      A3
ATOM  1268  C   ALA  167     46.982  56.694 -15.020  1.00 62.19      A3
ATOM  1269  O   ALA  167     47.719  56.000 -15.734  1.00 62.63      A3
ATOM  1270  N   VAL  168     47.210  58.011 -14.991  1.00 63.37      A3
ATOM  1271  H   VAL  168     46.756  58.570 -14.330  1.00  0.00      A3
ATOM  1272  CA  VAL  168     48.174  58.593 -15.923  1.00 65.62      A3
ATOM  1273  CB  VAL  168     48.061  60.121 -16.131  1.00 66.30      A3
ATOM  1274  CG1 VAL  168     46.687  60.431 -16.706  1.00 66.78      A3
ATOM  1275  CG2 VAL  168     48.278  60.879 -14.840  1.00 68.47      A3
ATOM  1276  C   VAL  168     49.579  58.339 -15.469  1.00 66.45      A3
ATOM  1277  O   VAL  168     50.458  58.183 -16.302  1.00 66.22      A3
ATOM  1278  N   LEU  169     49.823  58.241 -14.177  1.00 68.83      A3
ATOM  1279  H   LEU  169     49.102  58.404 -13.536  1.00  0.00      A3
ATOM  1280  CA  LEU  169     51.141  57.899 -13.695  1.00 71.81      A3
ATOM  1281  CB  LEU  169     51.249  58.228 -12.188  1.00 71.53      A3
ATOM  1282  CG  LEU  169     51.137  59.732 -11.813  1.00 70.68      A3
ATOM  1283  CD1 LEU  169     51.187  59.826 -10.298  1.00 69.39      A3
ATOM  1284  CD2 LEU  169     52.223  60.580 -12.491  1.00 68.49      A3
ATOM  1285  C   LEU  169     51.333  56.414 -13.979  1.00 73.61      A3
ATOM  1286  O   LEU  169     52.408  56.013 -14.429  1.00 74.75      A3
ATOM  1287  N   ARG  170     50.309  55.583 -13.819  1.00 75.45      A3
ATOM  1288  H   ARG  170     49.488  55.923 -13.399  1.00  0.00      A3
ATOM  1289  CA  ARG  170     50.364  54.179 -14.199  1.00 78.17      A3
ATOM  1290  CB  ARG  170     48.944  53.642 -14.004  1.00 78.45      A3
ATOM  1291  CG  ARG  170     48.394  52.506 -14.871  1.00 78.17      A3
ATOM  1292  CD  ARG  170     48.744  51.181 -14.271  1.00 77.25      A3
ATOM  1293  NE  ARG  170     48.123  51.120 -12.970  1.00 76.15      A3
ATOM  1294  HE  ARG  170     47.245  51.528 -12.824  1.00  0.00      A3
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FIG.5S

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ATOM 1295 CZ ARG 170 48.758 50.547 -11.970 1.00 76.14 A3
ATOM 1296 NH1 ARG 170 49.973 50.017 -12.112 1.00 76.84 A3
ATOM 1297 HH11 ARG 170 50.441 50.030 -12.994 1.00 0.00 A3
ATOM 1298 HH12 ARG 170 50.406 49.570 -11.329 1.00 0.00 A3
ATOM 1299 NH2 ARG 170 48.147 50.492 -10.806 1.00 77.02 A3
ATOM 1300 HH21 ARG 170 47.237 50.890 -10.714 1.00 0.00 A3
ATOM 1301 HH22 ARG 170 48.586 50.052 -10.023 1.00 0.00 A3
ATOM 1302 C ARG 170 50.870 54.052 -15.647 1.00 79.84 A3
ATOM 1303 O ARG 170 51.924 53.470 -15.908 1.00 80.07 A3
ATOM 1304 N HIS 171 50.193 54.663 -16.611 1.00 81.38 A3
ATOM 1305 H HIS 171 49.433 55.234 -16.359 1.00 0.00 A3
ATOM 1306 CA HIS 171 50.663 54.597 -17.970 1.00 84.03 A3
ATOM 1307 CB HIS 171 49.590 55.054 -18.902 1.00 86.82 A3
ATOM 1308 CG HIS 171 48.496 54.037 -19.147 1.00 90.73 A3
ATOM 1309 CD2 HIS 171 47.467 53.765 -18.272 1.00 91.35 A3
ATOM 1310 ND1 HIS 171 48.308 53.301 -20.248 1.00 92.24 A3
ATOM 1311 HD1 HIS 171 48.887 53.287 -21.044 1.00 0.00 A3
ATOM 1312 CE1 HIS 171 47.204 52.605 -20.077 1.00 92.41 A3
ATOM 1313 NE2 HIS 171 46.711 52.892 -18.891 1.00 92.59 A3
ATOM 1314 HE2 HIS 171 45.884 52.511 -18.518 1.00 0.00 A3
ATOM 1315 C HIS 171 51.907 55.446 -18.232 1.00 85.42 A3
ATOM 1316 O HIS 171 52.440 55.352 -19.344 1.00 85.98 A3
ATOM 1317 N LEU 172 52.359 56.307 -17.302 1.00 86.13 A3
ATOM 1318 H LEU 172 51.870 56.411 -16.463 1.00 0.00 A3
ATOM 1319 CA LEU 172 53.550 57.133 -17.496 1.00 86.02 A3
ATOM 1320 CB LEU 172 53.500 58.357 -16.607 1.00 86.31 A3
ATOM 1321 CG LEU 172 54.022 59.658 -17.203 1.00 87.48 A3
ATOM 1322 CD1 LEU 172 53.436 59.939 -18.596 1.00 87.68 A3
ATOM 1323 CD2 LEU 172 53.645 60.778 -16.251 1.00 87.95 A3
ATOM 1324 C LEU 172 54.813 56.357 -17.180 1.00 85.92 A3
ATOM 1325 O LEU 172 55.896 56.660 -17.692 1.00 86.23 A3
ATOM 1326 N ALA 173 54.733 55.383 -16.282 1.00 85.49 A3
ATOM 1327 H ALA 173 53.899 55.276 -15.769 1.00 0.00 A3
ATOM 1328 CA ALA 173 55.856 54.497 -16.087 1.00 85.65 A3
ATOM 1329 CB ALA 173 56.602 54.859 -14.809 1.00 85.01 A3
ATOM 1330 C ALA 173 55.330 53.073 -16.008 1.00 86.54 A3
ATOM 1331 OT1 ALA 173 55.585 52.347 -16.971 1.00 87.21 A3
ATOM 1332 OT2 ALA 173 54.650 52.707 -15.036 1.00 87.31 A3
ATOM 1333 CB LEU 210 45.234 42.591 25.453 1.00 52.47 B1
ATOM 1334 CG LEU 210 43.799 42.058 25.547 1.00 51.68 B1
ATOM 1335 CD1 LEU 210 43.123 42.562 26.804 1.00 53.37 B1
ATOM 1336 CD2 LEU 210 43.050 42.453 24.303 1.00 51.37 B1
ATOM 1337 C LEU 210 46.770 44.374 24.596 1.00 50.98 B1
ATOM 1338 O LEU 210 46.475 45.267 23.790 1.00 51.76 B1
ATOM 1339 HT1 LEU 210 44.382 44.922 24.421 1.00 0.00 B1
ATOM 1340 HT2 LEU 210 45.157 45.974 25.414 1.00 0.00 B1
ATOM 1341 N LEU 210 44.705 45.041 25.406 1.00 53.59 B1
ATOM 1342 HT3 LEU 210 43.855 45.012 25.997 1.00 0.00 B1
ATOM 1343 CA LEU 210 45.730 44.038 25.676 1.00 52.35 B1
ATOM 1344 N PRO 211 47.974 43.825 24.494 1.00 49.35 B1
ATOM 1345 CD PRO 211 48.621 43.024 25.532 1.00 49.52 B1
ATOM 1346 CA PRO 211 48.895 44.191 23.419 1.00 49.04 B1
ATOM 1347 CB PRO 211 50.209 43.571 23.865 1.00 49.02 B1
ATOM 1348 CG PRO 211 49.794 42.438 24.783 1.00 49.77 B1
ATOM 1349 C PRO 211 48.543 43.864 21.965 1.00 48.03 B1
ATOM 1350 O PRO 211 47.872 42.896 21.622 1.00 49.05 B1
ATOM 1351 N GLN 212 49.032 44.675 21.051 1.00 46.52 B1
ATOM 1352 H GLN 212 49.506 45.478 21.349 1.00 0.00 B1
ATOM 1353 CA GLN 212 48.839 44.461 19.641 1.00 45.47 B1
ATOM 1354 CB GLN 212 49.533 45.522 18.849 1.00 46.81 B1
ATOM 1355 CG GLN 212 48.482 46.139 17.999 1.00 49.55 B1
ATOM 1356 CD GLN 212 49.024 46.703 16.709 1.00 54.21 B1
ATOM 1357 OE1 GLN 212 48.429 47.672 16.232 1.00 57.72 B1
ATOM 1358 NE2 GLN 212 50.086 46.176 16.074 1.00 52.39 B1
ATOM 1359 HE21 GLN 212 50.530 45.383 16.430 1.00 0.00 B1
ATOM 1360 HE22 GLN 212 50.341 46.625 15.244 1.00 0.00 B1
ATOM 1361 C GLN 212 49.390 43.133 19.185 1.00 44.79 B1
ATOM 1362 O GLN 212 48.959 42.520 18.208 1.00 44.01 B1
ATOM 1363 N SER 213 50.401 42.671 19.893 1.00 44.72 B1
ATOM 1364 H SER 213 50.730 43.115 20.698 1.00 0.00 B1
ATOM 1365 CA SER 213 51.025 41.424 19.521 1.00 43.76 B1
ATOM 1366 CB SER 213 52.220 41.124 20.354 1.00 45.29 B1
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FIG.5T

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ATOM  1367 OG  SER  213      51.802  41.455  21.681  1.00 52.50      B1
ATOM  1368 HG  SER  213      52.479  41.127  22.288  1.00  0.00      B1
ATOM  1369 C   SER  213      50.014  40.376  19.784  1.00 40.92      B1
ATOM  1370 O   SER  213      49.964  39.492  18.947  1.00 43.32      B1
ATOM  1371 N   PHE  214      49.242  40.571  20.876  1.00 38.86      B1
ATOM  1372 H   PHE  214      49.414  41.370  21.410  1.00  0.00      B1
ATOM  1373 CA  PHE  214      48.210  39.664  21.336  1.00 37.40      B1
ATOM  1374 CB  PHE  214      47.568  40.064  22.634  1.00 37.45      B1
ATOM  1375 CG  PHE  214      46.494  39.080  23.035  1.00 41.01      B1
ATOM  1376 CD1 PHE  214      45.176  39.459  23.044  1.00 42.77      B1
ATOM  1377 CD2 PHE  214      46.818  37.794  23.400  1.00 42.02      B1
ATOM  1378 CE1 PHE  214      44.197  38.554  23.423  1.00 41.82      B1
ATOM  1379 CE2 PHE  214      45.834  36.898  23.776  1.00 41.70      B1
ATOM  1380 CZ  PHE  214      44.519  37.277  23.791  1.00 41.05      B1
ATOM  1381 C   PHE  214      47.109  39.656  20.321  1.00 36.54      B1
ATOM  1382 O   PHE  214      46.735  38.566  19.889  1.00 37.99      B1
ATOM  1383 N   LEU  215      46.616  40.812  19.893  1.00 33.27      B1
ATOM  1384 H   LEU  215      47.008  41.642  20.238  1.00  0.00      B1
ATOM  1385 CA  LEU  215      45.504  40.864  18.966  1.00 30.38      B1
ATOM  1386 CB  LEU  215      45.099  42.282  18.701  1.00 31.82      B1
ATOM  1387 CG  LEU  215      43.857  42.530  17.893  1.00 32.78      B1
ATOM  1388 CD1 LEU  215      42.727  41.963  18.737  1.00 32.95      B1
ATOM  1389 CD2 LEU  215      43.688  44.011  17.508  1.00 28.93      B1
ATOM  1390 C   LEU  215      45.811  40.232  17.648  1.00 29.57      B1
ATOM  1391 O   LEU  215      44.922  39.632  17.055  1.00 31.28      B1
ATOM  1392 N   LEU  216      47.031  40.379  17.155  1.00 29.44      B1
ATOM  1393 H   LEU  216      47.677  40.935  17.646  1.00  0.00      B1
ATOM  1394 CA  LEU  216      47.465  39.790  15.893  1.00 29.89      B1
ATOM  1395 CB  LEU  216      48.791  40.450  15.472  1.00 28.61      B1
ATOM  1396 CG  LEU  216      48.682  41.877  14.939  1.00 26.83      B1
ATOM  1397 CD1 LEU  216      49.925  42.558  15.344  1.00 28.57      B1
ATOM  1398 CD2 LEU  216      48.446  41.950  13.452  1.00 24.09      B1
ATOM  1399 C   LEU  216      47.613  38.274  16.062  1.00 31.23      B1
ATOM  1400 O   LEU  216      47.328  37.514  15.138  1.00 29.20      B1
ATOM  1401 N   LYS  217      47.999  37.826  17.261  1.00 32.50      B1
ATOM  1402 H   LYS  217      48.305  38.482  17.926  1.00  0.00      B1
ATOM  1403 CA  LYS  217      48.067  36.439  17.599  1.00 34.90      B1
ATOM  1404 CB  LYS  217      48.645  36.280  19.002  1.00 38.07      B1
ATOM  1405 CG  LYS  217      49.394  34.978  19.109  1.00 45.25      B1
ATOM  1406 CD  LYS  217      49.714  34.491  20.521  1.00 53.27      B1
ATOM  1407 CE  LYS  217      50.229  33.024  20.297  1.00 59.03      B1
ATOM  1408 NZ  LYS  217      50.213  32.135  21.467  1.00 62.10      B1
ATOM  1409 HZ1 LYS  217      49.239  32.056  21.824  1.00  0.00      B1
ATOM  1410 HZ2 LYS  217      50.830  32.515  22.214  1.00  0.00      B1
ATOM  1411 HZ3 LYS  217      50.554  31.195  21.179  1.00  0.00      B1
ATOM  1412 C   LYS  217      46.617  35.950  17.546  1.00 36.77      B1
ATOM  1413 O   LYS  217      46.311  34.933  16.886  1.00 39.58      B1
ATOM  1414 N   CYS  218      45.664  36.638  18.177  1.00 34.86      B1
ATOM  1415 H   CYS  218      45.907  37.388  18.751  1.00  0.00      B1
ATOM  1416 CA  CYS  218      44.277  36.238  18.076  1.00 33.61      B1
ATOM  1417 CB  CYS  218      43.430  37.175  18.846  1.00 33.21      B1
ATOM  1418 SG  CYS  218      43.856  36.710  20.515  1.00 35.92      B1
ATOM  1419 C   CYS  218      43.766  36.189  16.652  1.00 32.89      B1
ATOM  1420 O   CYS  218      43.155  35.169  16.323  1.00 34.71      B1
ATOM  1421 N   LEU  219      44.035  37.169  15.777  1.00 29.52      B1
ATOM  1422 H   LEU  219      44.512  37.960  16.104  1.00  0.00      B1
ATOM  1423 CA  LEU  219      43.614  37.119  14.393  1.00 27.44      B1
ATOM  1424 CB  LEU  219      44.116  38.412  13.727  1.00 26.24      B1
ATOM  1425 CG  LEU  219      43.884  38.768  12.241  1.00 25.07      B1
ATOM  1426 CD1 LEU  219      42.402  38.975  11.996  1.00 26.24      B1
ATOM  1427 CD2 LEU  219      44.563  40.051  11.882  1.00 22.10      B1
ATOM  1428 C   LEU  219      44.121  35.867  13.634  1.00 28.24      B1
ATOM  1429 O   LEU  219      43.373  35.204  12.889  1.00 27.12      B1
ATOM  1430 N   GLU  220      45.399  35.499  13.795  1.00 28.06      B1
ATOM  1431 H   GLU  220      45.957  35.974  14.448  1.00  0.00      B1
ATOM  1432 CA  GLU  220      45.963  34.411  13.048  1.00 28.38      B1
ATOM  1433 CB  GLU  220      47.376  34.198  13.469  1.00 34.25      B1
ATOM  1434 CG  GLU  220      48.049  33.079  12.666  1.00 46.36      B1
ATOM  1435 CD  GLU  220      49.545  32.794  12.907  1.00 55.51      B1
ATOM  1436 OE1 GLU  220      50.113  32.133  12.021  1.00 58.95      B1
ATOM  1437 OE2 GLU  220      50.144  33.213  13.930  1.00 60.41      B1
ATOM  1438 C   GLU  220      45.134  33.193  13.354  1.00 27.30      B1
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FIG.5U

ATOM 1439 O GLU 220 44.662 32.524 12.437 1.00 27.08 B1
ATOM 1440 N GLN 221 44.866 33.023 14.642 1.00 25.42 B1
ATOM 1441 H GLN 221 45.229 33.687 15.268 1.00 0.00 B1
ATOM 1442 CA GLN 221 44.074 31.940 15.176 1.00 26.28 B1
ATOM 1443 CB GLN 221 44.143 31.927 16.691 1.00 26.78 B1
ATOM 1444 CG GLN 221 45.555 31.456 17.011 1.00 29.19 B1
ATOM 1445 CD GLN 221 45.752 31.067 18.442 1.00 31.98 B1
ATOM 1446 OE1 GLN 221 46.472 30.162 18.808 1.00 35.98 B1
ATOM 1447 NE2 GLN 221 45.110 31.736 19.347 1.00 39.31 B1
ATOM 1448 HE21 GLN 221 45.263 31.423 20.246 1.00 0.00 B1
ATOM 1449 HE22 GLN 221 44.571 32.514 19.111 1.00 0.00 B1
ATOM 1450 C GLN 221 42.615 31.925 14.789 1.00 26.21 B1
ATOM 1451 O GLN 221 42.186 30.896 14.269 1.00 30.69 B1
ATOM 1452 N VAL 222 41.814 32.962 14.984 1.00 23.63 B1
ATOM 1453 H VAL 222 42.199 33.746 15.426 1.00 0.00 B1
ATOM 1454 CA VAL 222 40.429 33.034 14.537 1.00 21.92 B1
ATOM 1455 CB VAL 222 39.934 34.442 14.793 1.00 21.36 B1
ATOM 1456 CG1 VAL 222 38.706 34.831 14.027 1.00 17.72 B1
ATOM 1457 CG2 VAL 222 39.671 34.496 16.257 1.00 20.95 B1
ATOM 1458 C VAL 222 40.374 32.707 13.066 1.00 22.65 B1
ATOM 1459 O VAL 222 39.475 32.013 12.632 1.00 23.72 B1
ATOM 1460 N ARG 223 41.341 33.120 12.283 1.00 23.95 B1
ATOM 1461 H ARG 223 42.099 33.614 12.666 1.00 0.00 B1
ATOM 1462 CA ARG 223 41.309 32.939 10.844 1.00 27.19 B1
ATOM 1463 CB ARG 223 42.294 33.935 10.283 1.00 29.26 B1
ATOM 1464 CG ARG 223 42.102 34.364 8.869 1.00 35.23 B1
ATOM 1465 CD ARG 223 42.880 33.487 7.929 1.00 41.88 B1
ATOM 1466 NE ARG 223 41.972 32.676 7.096 1.00 47.42 B1
ATOM 1467 HE ARG 223 41.451 31.953 7.502 1.00 0.00 B1
ATOM 1468 CZ ARG 223 41.875 32.896 5.784 1.00 46.15 B1
ATOM 1469 NH1 ARG 223 42.575 33.837 5.246 1.00 49.54 B1
ATOM 1470 HH11 ARG 223 42.522 33.989 4.259 1.00 0.00 B1
ATOM 1471 HH12 ARG 223 43.156 34.428 5.805 1.00 0.00 B1
ATOM 1472 NH2 ARG 223 41.178 32.161 4.952 1.00 45.74 B1
ATOM 1473 HH21 ARG 223 40.697 31.353 5.290 1.00 0.00 B1
ATOM 1474 HH22 ARG 223 41.154 32.399 3.980 1.00 0.00 B1
ATOM 1475 C ARG 223 41.624 31.492 10.430 1.00 29.13 B1
ATOM 1476 O ARG 223 41.181 30.987 9.376 1.00 29.32 B1
ATOM 1477 N LYS 224 42.413 30.791 11.259 1.00 29.17 B1
ATOM 1478 H LYS 224 42.791 31.235 12.048 1.00 0.00 B1
ATOM 1479 CA LYS 224 42.714 29.411 10.994 1.00 27.70 B1
ATOM 1480 CB LYS 224 43.922 29.085 11.818 1.00 30.07 B1
ATOM 1481 CG LYS 224 44.372 27.660 11.706 1.00 36.70 B1
ATOM 1482 CD LYS 224 45.829 27.544 12.127 1.00 41.68 B1
ATOM 1483 CE LYS 224 46.303 26.478 11.131 1.00 48.18 B1
ATOM 1484 NZ LYS 224 47.750 26.492 10.913 1.00 53.57 B1
ATOM 1485 HZ1 LYS 224 48.230 26.241 11.801 1.00 0.00 B1
ATOM 1486 HZ2 LYS 224 48.057 27.436 10.606 1.00 0.00 B1
ATOM 1487 HZ3 LYS 224 47.998 25.792 10.183 1.00 0.00 B1
ATOM 1488 C LYS 224 41.464 28.598 11.347 1.00 26.27 B1
ATOM 1489 O LYS 224 40.970 27.810 10.510 1.00 24.82 B1
ATOM 1490 N ILE 225 40.892 28.835 12.547 1.00 24.75 B1
ATOM 1491 H ILE 225 41.308 29.487 13.151 1.00 0.00 B1
ATOM 1492 CA ILE 225 39.656 28.147 12.943 1.00 23.33 B1
ATOM 1493 CB ILE 225 39.146 28.622 14.296 1.00 18.08 B1
ATOM 1494 CG2 ILE 225 37.874 27.872 14.577 1.00 15.43 B1
ATOM 1495 CG1 ILE 225 40.161 28.400 15.380 1.00 13.38 B1
ATOM 1496 CD ILE 225 39.787 28.967 16.749 1.00 13.59 B1
ATOM 1497 C ILE 225 38.594 28.437 11.889 1.00 27.28 B1
ATOM 1498 O ILE 225 37.978 27.492 11.400 1.00 31.49 B1
ATOM 1499 N GLN 226 38.396 29.677 11.402 1.00 29.69 B1
ATOM 1500 H GLN 226 38.894 30.413 11.803 1.00 0.00 B1
ATOM 1501 CA GLN 226 37.450 29.969 10.313 1.00 29.12 B1
ATOM 1502 CB GLN 226 37.366 31.438 9.962 1.00 32.26 B1
ATOM 1503 CG GLN 226 36.682 32.156 11.108 1.00 36.28 B1
ATOM 1504 CD GLN 226 36.429 33.613 10.816 1.00 37.88 B1
ATOM 1505 OE1 GLN 226 37.158 34.281 10.076 1.00 36.34 B1
ATOM 1506 NE2 GLN 226 35.359 34.114 11.421 1.00 39.62 B1
ATOM 1507 HE21 GLN 226 34.823 33.501 11.971 1.00 0.00 B1
ATOM 1508 HE22 GLN 226 35.153 35.057 11.287 1.00 0.00 B1
ATOM 1509 C GLN 226 37.714 29.295 9.007 1.00 26.82 B1
ATOM 1510 O GLN 226 36.775 28.887 8.325 1.00 27.45 B1

FIG.5V

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ATOM  1511  N   GLY  227      38.940  29.186   8.570  1.00 26.55      B1
ATOM  1512  H   GLY  227      39.688  29.612   9.043  1.00  0.00      B1
ATOM  1513  CA  GLY  227      39.195  28.427   7.348  1.00 27.27      B1
ATOM  1514  C   GLY  227      38.832  26.949   7.574  1.00 27.65      B1
ATOM  1515  O   GLY  227      38.287  26.291   6.656  1.00 26.79      B1
ATOM  1516  N   ASP  228      39.025  26.429   8.819  1.00 27.03      B1
ATOM  1517  H   ASP  228      39.460  26.957   9.523  1.00  0.00      B1
ATOM  1518  CA  ASP  228      38.618  25.038   9.052  1.00 28.20      B1
ATOM  1519  CB  ASP  228      38.986  24.492  10.391  1.00 26.04      B1
ATOM  1520  CG  ASP  228      40.427  24.554  10.774  1.00 24.88      B1
ATOM  1521  OD1 ASP  228      40.627  24.521  11.977  1.00 23.37      B1
ATOM  1522  OD2 ASP  228      41.302  24.637   9.912  1.00 23.32      B1
ATOM  1523  C   ASP  228      37.120  24.830   8.992  1.00 27.23      B1
ATOM  1524  O   ASP  228      36.662  23.900   8.336  1.00 27.07      B1
ATOM  1525  N   GLY  229      36.390  25.739   9.639  1.00 26.74      B1
ATOM  1526  H   GLY  229      36.861  26.444  10.134  1.00  0.00      B1
ATOM  1527  CA  GLY  229      34.946  25.723   9.673  1.00 25.87      B1
ATOM  1528  C   GLY  229      34.393  25.825   8.274  1.00 24.95      B1
ATOM  1529  O   GLY  229      33.370  25.222   7.956  1.00 25.73      B1
ATOM  1530  N   ALA  230      35.058  26.541   7.391  1.00 23.97      B1
ATOM  1531  H   ALA  230      35.871  27.026   7.654  1.00  0.00      B1
ATOM  1532  CA  ALA  230      34.530  26.688   6.061  1.00 25.94      B1
ATOM  1533  CB  ALA  230      35.193  27.852   5.312  1.00 19.76      B1
ATOM  1534  C   ALA  230      34.794  25.403   5.304  1.00 29.42      B1
ATOM  1535  O   ALA  230      34.014  25.061   4.423  1.00 32.07      B1
ATOM  1536  N   ALA  231      35.878  24.671   5.572  1.00 32.16      B1
ATOM  1537  H   ALA  231      36.556  25.045   6.175  1.00  0.00      B1
ATOM  1538  CA  ALA  231      36.141  23.364   4.957  1.00 31.99      B1
ATOM  1539  CB  ALA  231      37.489  22.847   5.428  1.00 32.77      B1
ATOM  1540  C   ALA  231      35.060  22.361   5.386  1.00 32.99      B1
ATOM  1541  O   ALA  231      34.599  21.575   4.576  1.00 34.12      B1
ATOM  1542  N   LEU  232      34.662  22.309   6.652  1.00 33.30      B1
ATOM  1543  H   LEU  232      35.174  22.861   7.284  1.00  0.00      B1
ATOM  1544  CA  LEU  232      33.558  21.506   7.165  1.00 35.33      B1
ATOM  1545  CB  LEU  232      33.279  21.783   8.626  1.00 34.22      B1
ATOM  1546  CG  LEU  232      32.410  20.861   9.394  1.00 33.16      B1
ATOM  1547  CD1 LEU  232      33.191  19.545   9.451  1.00 34.59      B1
ATOM  1548  CD2 LEU  232      32.107  21.381  10.800  1.00 31.32      B1
ATOM  1549  C   LEU  232      32.271  21.829   6.440  1.00 36.65      B1
ATOM  1550  O   LEU  232      31.703  20.986   5.749  1.00 36.42      B1
ATOM  1551  N   GLN  233      31.836  23.084   6.570  1.00 38.89      B1
ATOM  1552  H   GLN  233      32.378  23.719   7.087  1.00  0.00      B1
ATOM  1553  CA  GLN  233      30.637  23.579   5.933  1.00 40.02      B1
ATOM  1554  CB  GLN  233      30.572  25.072   6.162  1.00 42.25      B1
ATOM  1555  CG  GLN  233      30.290  25.398   7.626  1.00 48.22      B1
ATOM  1556  CD  GLN  233      30.021  26.879   7.983  1.00 53.75      B1
ATOM  1557  OE1 GLN  233      30.799  27.810   7.718  1.00 55.93      B1
ATOM  1558  NE2 GLN  233      28.909  27.215   8.634  1.00 56.51      B1
ATOM  1559 HE21 GLN  233      28.810  28.144   8.902  1.00  0.00      B1
ATOM  1560 HE22 GLN  233      28.205  26.533   8.710  1.00  0.00      B1
ATOM  1561  C   GLN  233      30.635  23.243   4.441  1.00 39.70      B1
ATOM  1562  O   GLN  233      29.631  22.777   3.898  1.00 40.20      B1
ATOM  1563  N   GLU  234      31.744  23.377   3.736  1.00 39.32      B1
ATOM  1564  H   GLU  234      32.544  23.750   4.163  1.00  0.00      B1
ATOM  1565  CA  GLU  234      31.809  23.025   2.329  1.00 39.23      B1
ATOM  1566  CB  GLU  234      33.155  23.434   1.811  1.00 40.25      B1
ATOM  1567  CG  GLU  234      33.292  23.028   0.383  1.00 47.69      B1
ATOM  1568  CD  GLU  234      34.733  23.056  -0.073  1.00 53.40      B1
ATOM  1569  OE1 GLU  234      34.986  23.721  -1.100  1.00 53.78      B1
ATOM  1570  OE2 GLU  234      35.568  22.400   0.590  1.00 57.55      B1
ATOM  1571  C   GLU  234      31.580  21.535   2.136  1.00 37.09      B1
ATOM  1572  O   GLU  234      30.884  21.217   1.188  1.00 36.67      B1
ATOM  1573  N   LYS  235      32.092  20.623   2.986  1.00 37.27      B1
ATOM  1574  H   LYS  235      32.668  20.965   3.706  1.00  0.00      B1
ATOM  1575  CA  LYS  235      31.832  19.177   2.942  1.00 36.27      B1
ATOM  1576  CB  LYS  235      32.516  18.365   3.997  1.00 34.92      B1
ATOM  1577  CG  LYS  235      33.978  18.483   4.107  1.00 38.47      B1
ATOM  1578  CD  LYS  235      34.762  17.999   2.921  1.00 38.07      B1
ATOM  1579  CE  LYS  235      36.192  18.051   3.460  1.00 39.15      B1
ATOM  1580  NZ  LYS  235      37.117  17.460   2.521  1.00 41.34      B1
ATOM  1581 HZ1 LYS  235      37.080  17.978   1.622  1.00  0.00      B1
ATOM  1582 HZ2 LYS  235      36.854  16.466   2.363  1.00  0.00      B1
```

FIG.5W

```
ATOM  1583 HZ3 LYS  235      38.080  17.497   2.911  1.00  0.00      B1
ATOM  1584  C  LYS  235      30.363  18.847   3.204  1.00 35.20      B1
ATOM  1585  O  LYS  235      29.722  18.102   2.463  1.00 35.60      B1
ATOM  1586  N  LEU  236      29.807  19.332   4.301  1.00 33.53      B1
ATOM  1587  H  LEU  236      30.363  19.888   4.885  1.00  0.00      B1
ATOM  1588 CA  LEU  236      28.417  19.116   4.641  1.00 32.30      B1
ATOM  1589 CB  LEU  236      28.093  19.918   5.894  1.00 28.85      B1
ATOM  1590 CG  LEU  236      28.791  19.441   7.148  1.00 28.23      B1
ATOM  1591 CD1 LEU  236      28.703  20.460   8.268  1.00 24.14      B1
ATOM  1592 CD2 LEU  236      28.132  18.163   7.587  1.00 26.66      B1
ATOM  1593  C  LEU  236      27.590  19.574   3.453  1.00 33.69      B1*
ATOM  1594  O  LEU  236      26.691  18.849   3.064  1.00 35.13      B1
ATOM  1595  N  CYS  237      27.870  20.670   2.753  1.00 34.49      B1
ATOM  1596  H  CYS  237      28.611  21.251   3.025  1.00  0.00      B1
ATOM  1597 CA  CYS  237      27.064  21.016   1.606  1.00 34.95      B1
ATOM  1598  C  CYS  237      27.324  20.090   0.451  1.00 35.97      B1
ATOM  1599  O  CYS  237      26.360  19.573  -0.089  1.00 36.09      B1
ATOM  1600 CB  CYS  237      27.334  22.413   1.130  1.00 35.18      B1
ATOM  1601 SG  CYS  237      26.409  22.880  -0.365  1.00 36.40      B1
ATOM  1602  N  ALA  238      28.571  19.804   0.074  1.00 37.29      B1
ATOM  1603  H  ALA  238      29.324  20.158   0.591  1.00  0.00      B1
ATOM  1604 CA  ALA  238      28.841  18.973  -1.090  1.00 36.80      B1
ATOM  1605 CB  ALA  238      30.274  18.684  -1.403  1.00 37.35      B1
ATOM  1606  C  ALA  238      28.320  17.617  -0.911  1.00 36.49      B1
ATOM  1607  O  ALA  238      27.645  17.198  -1.809  1.00 36.54      B1
ATOM  1608  N  THR  239      28.628  16.969   0.193  1.00 38.80      B1
ATOM  1609  H  THR  239      29.236  17.391   0.821  1.00  0.00      B1
ATOM  1610 CA  THR  239      28.230  15.587   0.464  1.00 41.33      B1
ATOM  1611 CB  THR  239      29.158  15.035   1.554  1.00 42.38      B1
ATOM  1612 OG1 THR  239      30.473  15.265   1.031  1.00 45.70      B1
ATOM  1613 HG1 THR  239      31.019  15.668   1.709  1.00  0.00      B1
ATOM  1614 CG2 THR  239      28.936  13.574   1.916  1.00 41.85      B1
ATOM  1615  C  THR  239      26.771  15.341   0.864  1.00 41.94      B1
ATOM  1616  O  THR  239      26.260  14.284   0.460  1.00 43.34      B1
ATOM  1617  N  TYR  240      26.095  16.207   1.669  1.00 40.07      B1
ATOM  1618  H  TYR  240      26.538  17.034   1.953  1.00  0.00      B1
ATOM  1619 CA  TYR  240      24.718  15.992   2.084  1.00 38.21      B1
ATOM  1620 CB  TYR  240      24.594  15.993   3.618  1.00 38.08      B1
ATOM  1621 CG  TYR  240      25.524  14.926   4.193  1.00 43.37      B1
ATOM  1622 CD1 TYR  240      26.475  15.243   5.149  1.00 45.06      B1
ATOM  1623 CE1 TYR  240      27.420  14.283   5.529  1.00 47.35      B1
ATOM  1624 CD2 TYR  240      25.518  13.643   3.641  1.00 43.89      B1
ATOM  1625 CE2 TYR  240      26.442  12.690   4.003  1.00 44.77      B1
ATOM  1626  CZ  TYR  240      27.410  13.005   4.943  1.00 47.96      B1
ATOM  1627  OH  TYR  240      28.390  12.047   5.244  1.00 46.59      B1
ATOM  1628  HH  TYR  240      28.027  11.187   4.992  1.00  0.00      B1
ATOM  1629  C  TYR  240      23.781  17.032   1.516  1.00 39.49      B1
ATOM  1630  O  TYR  240      22.587  16.934   1.775  1.00 42.76      B1
ATOM  1631  N  LYS  241      24.174  18.011   0.694  1.00 37.36      B1
ATOM  1632  H  LYS  241      25.091  18.023   0.345  1.00  0.00      B1
ATOM  1633 CA  LYS  241      23.314  19.115   0.275  1.00 36.37      B1
ATOM  1634 CB  LYS  241      22.173  18.648  -0.595  1.00 38.38      B1
ATOM  1635 CG  LYS  241      22.645  17.940  -1.838  1.00 42.94      B1
ATOM  1636 CD  LYS  241      23.468  18.809  -2.737  1.00 46.97      B1
ATOM  1637 CE  LYS  241      23.657  18.070  -4.051  1.00 49.20      B1
ATOM  1638 NZ  LYS  241      22.509  18.372  -4.893  1.00 51.54      B1
ATOM  1639 HZ1 LYS  241      22.447  19.400  -5.038  1.00  0.00      B1
ATOM  1640 HZ2 LYS  241      21.641  18.041  -4.426  1.00  0.00      B1
ATOM  1641 HZ3 LYS  241      22.609  17.895  -5.811  1.00  0.00      B1
ATOM  1642  C  LYS  241      22.720  19.904   1.429  1.00 33.37      B1
ATOM  1643  O  LYS  241      21.728  20.580   1.223  1.00 33.90      B1
ATOM  1644  N  LEU  242      23.286  19.853   2.648  1.00 31.40      B1
ATOM  1645  H  LEU  242      24.055  19.260   2.756  1.00  0.00      B1
ATOM  1646 CA  LEU  242      22.904  20.682   3.758  1.00 31.09      B1
ATOM  1647 CB  LEU  242      23.253  20.059   5.096  1.00 28.55      B1
ATOM  1648 CG  LEU  242      22.571  18.798   5.641  1.00 30.36      B1
ATOM  1649 CD1 LEU  242      22.530  18.814   7.138  1.00 29.62      B1
ATOM  1650 CD2 LEU  242      21.086  18.861   5.443  1.00 31.94      B1
ATOM  1651  C  LEU  242      23.778  21.933   3.550  1.00 34.03      B1
ATOM  1652  O  LEU  242      24.903  22.027   4.058  1.00 35.53      B1
ATOM  1653  N  CYS  243      23.316  22.883   2.722  1.00 34.89      B1
ATOM  1654  H  CYS  243      22.491  22.665   2.238  1.00  0.00      B1
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FIG.5X

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ATOM  1655 CA  CYS  243     24.051  24.083   2.377  1.00 35.42      B1
ATOM  1656 C   CYS  243     23.492  25.335   2.975  1.00 36.85      B1
ATOM  1657 O   CYS  243     23.956  26.400   2.565  1.00 40.10      B1
ATOM  1658 CB  CYS  243     24.046  24.383   0.929  1.00 33.12      B1
ATOM  1659 SG  CYS  243     24.438  22.883   0.099  1.00 38.25      B1
ATOM  1660 N   HIS  244     22.496  25.393   3.848  1.00 35.37      B1
ATOM  1661 H   HIS  244     22.185  24.588   4.318  1.00  0.00      B1
ATOM  1662 CA  HIS  244     21.939  26.676   4.191  1.00 33.29      B1
ATOM  1663 CB  HIS  244     20.655  26.987   3.340  1.00 33.64      B1
ATOM  1664 CG  HIS  244     20.915  27.205   1.857  1.00 33.12      B1
ATOM  1665 CD2 HIS  244     20.288  26.584   0.814  1.00 37.29      B1
ATOM  1666 ND1 HIS  244     21.874  27.902   1.298  1.00 36.85      B1
ATOM  1667 HD1 HIS  244     22.648  28.281   1.778  1.00  0.00      B1
ATOM  1668 CE1 HIS  244     21.874  27.722  -0.013  1.00 35.95      B1
ATOM  1669 NE2 HIS  244     20.910  26.920  -0.301  1.00 35.54      B1
ATOM  1670 HE2 HIS  244     20.616  26.706  -1.214  1.00  0.00      B1
ATOM  1671 C   HIS  244     21.621  26.565   5.650  1.00 33.38      B1
ATOM  1672 O   HIS  244     20.546  26.105   6.029  1.00 33.23      B1
ATOM  1673 N   PRO  245     22.539  27.018   6.499  1.00 33.21      B1
ATOM  1674 CD  PRO  245     23.851  27.524   6.099  1.00 31.29      B1
ATOM  1675 CA  PRO  245     22.373  26.979   7.948  1.00 34.16      B1
ATOM  1676 CB  PRO  245     23.490  27.799   8.467  1.00 32.85      B1
ATOM  1677 CG  PRO  245     24.564  27.549   7.428  1.00 31.74      B1
ATOM  1678 C   PRO  245     21.032  27.470   8.407  1.00 36.26      B1
ATOM  1679 O   PRO  245     20.478  26.878   9.315  1.00 38.13      B1
ATOM  1680 N   GLU  246     20.529  28.463   7.640  1.00 39.64      B1
ATOM  1681 H   GLU  246     21.134  28.747   6.934  1.00  0.00      B1
ATOM  1682 CA  GLU  246     19.257  29.229   7.711  1.00 41.10      B1
ATOM  1683 CB  GLU  246     19.044  30.107   6.438  1.00 43.15      B1
ATOM  1684 CG  GLU  246     20.256  30.918   5.944  1.00 47.07      B1
ATOM  1685 CD  GLU  246     20.813  30.539   4.558  1.00 52.63      B1
ATOM  1686 OE1 GLU  246     22.054  30.545   4.374  1.00 54.22      B1
ATOM  1687 OE2 GLU  246     20.002  30.250   3.656  1.00 53.39      B1
ATOM  1688 C   GLU  246     18.071  28.298   7.819  1.00 40.57      B1
ATOM  1689 O   GLU  246     17.308  28.338   8.791  1.00 39.90      B1
ATOM  1690 N   GLU  247     18.025  27.388   6.840  1.00 40.32      B1
ATOM  1691 H   GLU  247     18.750  27.334   6.190  1.00  0.00      B1
ATOM  1692 CA  GLU  247     17.001  26.347   6.830  1.00 40.76      B1
ATOM  1693 CB  GLU  247     17.139  25.423   5.642  1.00 44.03      B1
ATOM  1694 CG  GLU  247     16.830  26.240   4.400  1.00 48.54      B1
ATOM  1695 CD  GLU  247     17.163  25.628   3.050  1.00 50.24      B1
ATOM  1696 OE1 GLU  247     16.849  26.299   2.056  1.00 52.92      B1
ATOM  1697 OE2 GLU  247     17.744  24.533   2.987  1.00 50.84      B1
ATOM  1698 C   GLU  247     16.966  25.444   8.034  1.00 39.24      B1
ATOM  1699 O   GLU  247     15.915  24.888   8.329  1.00 39.40      B1
ATOM  1700 N   LEU  248     18.066  25.280   8.760  1.00 37.92      B1
ATOM  1701 H   LEU  248     18.864  25.814   8.576  1.00  0.00      B1
ATOM  1702 CA  LEU  248     18.101  24.338   9.858  1.00 35.75      B1
ATOM  1703 CB  LEU  248     19.458  23.623   9.796  1.00 34.13      B1
ATOM  1704 CG  LEU  248     19.669  22.866   8.430  1.00 34.00      B1
ATOM  1705 CD1 LEU  248     20.997  22.149   8.306  1.00 33.97      B1
ATOM  1706 CD2 LEU  248     18.620  21.810   8.322  1.00 32.33      B1
ATOM  1707 C   LEU  248     17.871  25.031  11.155  1.00 36.51      B1
ATOM  1708 O   LEU  248     17.736  24.370  12.186  1.00 36.31      B1
ATOM  1709 N   VAL  249     17.663  26.350  11.146  1.00 38.88      B1
ATOM  1710 H   VAL  249     17.566  26.810  10.283  1.00  0.00      B1
ATOM  1711 CA  VAL  249     17.573  27.133  12.371  1.00 41.39      B1
ATOM  1712 CB  VAL  249     17.265  28.640  12.020  1.00 43.72      B1
ATOM  1713 CG1 VAL  249     15.804  28.985  11.776  1.00 44.70      B1
ATOM  1714 CG2 VAL  249     17.702  29.434  13.214  1.00 45.20      B1
ATOM  1715 C   VAL  249     16.590  26.635  13.406  1.00 42.61      B1
ATOM  1716 O   VAL  249     16.912  26.716  14.594  1.00 44.77      B1
ATOM  1717 N   LEU  250     15.453  26.035  13.016  1.00 43.61      B1
ATOM  1718 H   LEU  250     15.319  25.919  12.053  1.00  0.00      B1
ATOM  1719 CA  LEU  250     14.457  25.537  13.987  1.00 43.96      B1
ATOM  1720 CB  LEU  250     13.102  25.296  13.373  1.00 43.88      B1
ATOM  1721 CG  LEU  250     12.729  26.281  12.313  1.00 47.04      B1
ATOM  1722 CD1 LEU  250     13.092  25.577  11.011  1.00 47.30      B1
ATOM  1723 CD2 LEU  250     11.286  26.772  12.441  1.00 46.18      B1
ATOM  1724 C   LEU  250     14.852  24.207  14.626  1.00 43.96      B1
ATOM  1725 O   LEU  250     14.450  23.887  15.764  1.00 44.07      B1
ATOM  1726 N   LEU  251     15.691  23.446  13.893  1.00 42.41      B1
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FIG.5Y

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ATOM  1727  H  LEU  251    16.049  23.788  13.048  1.00  0.00    B1
ATOM  1728  CA LEU  251    16.155  22.159  14.362  1.00 40.63    B1
ATOM  1729  CB LEU  251    16.834  21.418  13.257  1.00 36.17    B1
ATOM  1730  CG LEU  251    15.996  20.629  12.267  1.00 33.16    B1
ATOM  1731  CD1 LEU  251   14.595  21.168  11.956  1.00 33.36    B1
ATOM  1732  CD2 LEU  251   16.875  20.619  11.050  1.00 34.71    B1
ATOM  1733  C  LEU  251    17.104  22.372  15.493  1.00 42.78    B1
ATOM  1734  O  LEU  251    17.124  21.554  16.395  1.00 45.44    B1
ATOM  1735  N  GLY  252    17.826  23.477  15.610  1.00 44.86    B1
ATOM  1736  H  GLY  252    17.750  24.160  14.910  1.00  0.00    B1
ATOM  1737  CA GLY  252    18.734  23.711  16.719  1.00 46.68    B1
ATOM  1738  C  GLY  252    18.071  23.596  18.067  1.00 49.18    B1
ATOM  1739  O  GLY  252    18.709  23.318  19.077  1.00 49.23    B1
ATOM  1740  N  HIS  253    16.756  23.787  18.046  1.00 53.74    B1
ATOM  1741  H  HIS  253    16.358  24.055  17.190  1.00  0.00    B1
ATOM  1742  CA HIS  253    15.859  23.649  19.197  1.00 57.46    B1
ATOM  1743  CB HIS  253    14.468  24.157  18.764  1.00 62.93    B1
ATOM  1744  CG HIS  253    13.212  23.813  19.577  1.00 68.75    B1
ATOM  1745  CD2 HIS  253    12.031  24.529  19.414  1.00 71.00    B1
ATOM  1746  ND1 HIS  253    12.980  22.854  20.479  1.00 70.67    B1
ATOM  1747  HD1 HIS  253    13.627  22.193  20.830  1.00  0.00    B1
ATOM  1748  CE1 HIS  253    11.723  22.966  20.845  1.00 73.40    B1
ATOM  1749  NE2 HIS  253    11.156  23.973  20.204  1.00 72.91    B1
ATOM  1750  HE2 HIS  253    10.218  24.260  20.311  1.00  0.00    B1
ATOM  1751  C  HIS  253    15.771  22.209  19.691  1.00 56.06    B1
ATOM  1752  O  HIS  253    15.880  21.827  20.857  1.00 56.17    B1
ATOM  1753  N  SER  254    15.395  21.435  18.724  1.00 53.46    B1
ATOM  1754  H  SER  254    15.278  21.783  17.813  1.00  0.00    B1
ATOM  1755  CA SER  254    15.177  20.034  18.898  1.00 52.61    B1
ATOM  1756  CB SER  254    14.613  19.595  17.576  1.00 53.04    B1
ATOM  1757  OG SER  254    13.793  20.686  17.158  1.00 56.04    B1
ATOM  1758  HG SER  254    13.369  20.467  16.319  1.00  0.00    B1
ATOM  1759  C  SER  254    16.512  19.386  19.275  1.00 51.48    B1
ATOM  1760  O  SER  254    16.596  18.639  20.245  1.00 51.90    B1
ATOM  1761  N  LEU  255    17.577  19.790  18.562  1.00 49.31    B1
ATOM  1762  H  LEU  255    17.430  20.480  17.889  1.00  0.00    B1
ATOM  1763  CA LEU  255    18.913  19.272  18.723  1.00 46.02    B1
ATOM  1764  CB LEU  255    19.706  19.723  17.537  1.00 44.66    B1
ATOM  1765  CG LEU  255    19.362  18.968  16.274  1.00 44.51    B1
ATOM  1766  CD1 LEU  255    19.810  19.679  15.006  1.00 43.16    B1
ATOM  1767  CD2 LEU  255    19.969  17.604  16.456  1.00 44.67    B1
ATOM  1768  C  LEU  255    19.536  19.718  20.012  1.00 46.56    B1
ATOM  1769  O  LEU  255    20.565  19.174  20.440  1.00 46.82    B1
ATOM  1770  N  GLY  256    18.918  20.759  20.581  1.00 45.93    B1
ATOM  1771  H  GLY  256    18.210  21.225  20.101  1.00  0.00    B1
ATOM  1772  CA GLY  256    19.277  21.273  21.890  1.00 46.68    B1
ATOM  1773  C  GLY  256    20.669  21.866  21.970  1.00 47.28    B1
ATOM  1774  O  GLY  256    21.273  21.844  23.056  1.00 49.64    B1
ATOM  1775  N  ILE  257    21.143  22.441  20.849  1.00 45.74    B1
ATOM  1776  H  ILE  257    20.497  22.589  20.128  1.00  0.00    B1
ATOM  1777  CA ILE  257    22.481  23.017  20.726  1.00 43.64    B1
ATOM  1778  CB ILE  257    22.684  23.363  19.257  1.00 42.54    B1
ATOM  1779  CG2 ILE  257    23.988  24.110  19.073  1.00 41.05    B1
ATOM  1780  CG1 ILE  257    22.694  22.088  18.437  1.00 40.55    B1
ATOM  1781  CD ILE  257    22.452  22.468  16.970  1.00 39.49    B1
ATOM  1782  C  ILE  257    22.559  24.246  21.616  1.00 43.27    B1
ATOM  1783  O  ILE  257    21.706  25.110  21.450  1.00 43.22    B1
ATOM  1784  N  PRO  258    23.441  24.392  22.608  1.00 43.05    B1
ATOM  1785  CD PRO  258    24.133  23.321  23.296  1.00 43.29    B1
ATOM  1786  CA PRO  258    23.559  25.616  23.360  1.00 43.82    B1
ATOM  1787  CB PRO  258    24.295  25.236  24.612  1.00 41.97    B1
ATOM  1788  CG PRO  258    25.107  24.064  24.186  1.00 43.79    B1
ATOM  1789  C  PRO  258    24.252  26.703  22.555  1.00 46.06    B1
ATOM  1790  O  PRO  258    24.983  26.513  21.560  1.00 46.59    B1
ATOM  1791  N  TRP  259    23.996  27.887  23.106  1.00 46.75    B1
ATOM  1792  H  TRP  259    23.588  27.921  23.994  1.00  0.00    B1
ATOM  1793  CA TRP  259    24.427  29.143  22.517  1.00 45.77    B1
ATOM  1794  CB TRP  259    23.213  30.071  22.397  1.00 46.60    B1
ATOM  1795  CG TRP  259    23.556  31.372  21.749  1.00 47.51    B1
ATOM  1796  CD2 TRP  259    23.860  31.525  20.430  1.00 47.83    B1
ATOM  1797  CE2 TRP  259    24.154  32.888  20.392  1.00 48.47    B1
ATOM  1798  CE3 TRP  259    23.940  30.745  19.290  1.00 47.39    B1
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FIG.5Z

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ATOM 1799 CD1 TRP 259 23.639 32.520 22.493 1.00 48.60 B1
ATOM 1800 NE1 TRP 259 24.013 33.421 21.628 1.00 48.27 B1
ATOM 1801 HE1 TRP 259 24.224 34.344 21.870 1.00 0.00 B1
ATOM 1802 CZ2 TRP 259 24.531 33.486 19.195 1.00 47.40 B1
ATOM 1803 CZ3 TRP 259 24.317 31.344 18.097 1.00 49.07 B1
ATOM 1804 CH2 TRP 259 24.613 32.706 18.050 1.00 49.12 B1
ATOM 1805 C TRP 259 25.459 29.727 23.440 1.00 44.01 B1
ATOM 1806 O TRP 259 25.340 29.664 24.671 1.00 43.25 B1
ATOM 1807 N ALA 260 26.469 30.247 22.777 1.00 43.01 B1
ATOM 1808 H ALA 260 26.523 30.198 21.796 1.00 0.00 B1
ATOM 1809 CA ALA 260 27.493 30.973 23.482 1.00 43.48 B1
ATOM 1810 CB ALA 260 28.874 30.549 22.969 1.00 43.33 B1
ATOM 1811 C ALA 260 27.249 32.486 23.216 1.00 43.41 B1
ATOM 1812 O ALA 260 27.315 32.946 22.054 1.00 40.55 B1
ATOM 1813 N PRO 261 26.853 33.267 24.253 1.00 42.61 B1
ATOM 1814 CD PRO 261 26.527 32.807 25.606 1.00 42.33 B1
ATOM 1815 CA PRO 261 26.720 34.701 24.199 1.00 42.37 B1
ATOM 1816 CB PRO 261 25.778 34.987 25.335 1.00 41.46 B1
ATOM 1817 CG PRO 261 26.251 34.060 26.411 1.00 40.00 B1
ATOM 1818 C PRO 261 28.087 35.369 24.311 1.00 42.22 B1
ATOM 1819 O PRO 261 28.988 34.956 25.037 1.00 38.82 B1
ATOM 1820 N LEU 262 28.234 36.403 23.486 1.00 45.20 B1
ATOM 1821 H LEU 262 27.513 36.610 22.853 1.00 0.00 B1
ATOM 1822 CA LEU 262 29.434 37.210 23.498 1.00 46.50 B1
ATOM 1823 CB LEU 262 30.531 36.609 22.610 1.00 45.09 B1
ATOM 1824 CG LEU 262 31.903 37.157 22.964 1.00 42.55 B1
ATOM 1825 CD1 LEU 262 32.344 36.695 24.338 1.00 41.52 B1
ATOM 1826 CD2 LEU 262 32.850 36.730 21.900 1.00 44.21 B1
ATOM 1827 C LEU 262 29.154 38.628 23.035 1.00 48.56 B1
ATOM 1828 O LEU 262 29.633 39.470 23.790 1.00 48.23 B1
ATOM 1829 N SER 263 28.388 38.956 21.960 1.00 51.33 B1
ATOM 1830 H SER 263 27.982 38.242 21.427 1.00 0.00 B1
ATOM 1831 CA SER 263 28.127 40.339 21.494 1.00 55.19 B1
ATOM 1832 CB SER 263 26.871 40.511 20.612 1.00 57.17 B1
ATOM 1833 OG SER 263 26.498 39.411 19.776 1.00 64.12 B1
ATOM 1834 HG SER 263 26.093 38.741 20.336 1.00 0.00 B1
ATOM 1835 C SER 263 27.909 41.354 22.600 1.00 56.15 B1
ATOM 1836 O SER 263 28.744 42.243 22.753 1.00 57.88 B1
ATOM 1837 N SER 264 26.899 41.231 23.452 1.00 56.52 B1
ATOM 1838 H SER 264 26.277 40.478 23.415 1.00 0.00 B1
ATOM 1839 CA SER 264 26.716 42.204 24.494 1.00 58.28 B1
ATOM 1840 CB SER 264 25.313 41.977 25.064 1.00 58.77 B1
ATOM 1841 OG SER 264 25.099 40.726 25.713 1.00 58.50 B1
ATOM 1842 HG SER 264 25.385 40.832 26.632 1.00 0.00 B1
ATOM 1843 C SER 264 27.800 42.168 25.584 1.00 59.95 B1
ATOM 1844 O SER 264 27.610 42.805 26.620 1.00 60.44 B1
ATOM 1845 N CYS 265 28.948 41.484 25.466 1.00 61.37 B1
ATOM 1846 H CYS 265 29.192 41.114 24.596 1.00 0.00 B1
ATOM 1847 CA CYS 265 29.958 41.502 26.509 1.00 62.57 B1
ATOM 1848 CB CYS 265 30.991 40.418 26.285 1.00 64.32 B1
ATOM 1849 SG CYS 265 32.322 40.638 27.504 1.00 71.40 B1
ATOM 1850 C CYS 265 30.667 42.860 26.515 1.00 63.12 B1
ATOM 1851 OT1 CYS 265 31.065 43.360 25.444 1.00 63.44 B1
ATOM 1852 OT2 CYS 265 30.809 43.408 27.610 1.00 61.72 B1
ATOM 1853 CB ALA 272 40.020 43.327 30.788 1.00 77.44 B2
ATOM 1854 C ALA 272 38.698 41.201 30.601 1.00 76.53 B2
ATOM 1855 O ALA 272 37.525 40.873 30.361 1.00 76.81 B2
ATOM 1856 HT1 ALA 272 37.486 43.550 30.261 1.00 0.00 B2
ATOM 1857 HT2 ALA 272 37.357 42.450 28.996 1.00 0.00 B2
ATOM 1858 N ALA 272 37.973 43.169 29.427 1.00 76.81 B2
ATOM 1859 HT3 ALA 272 38.195 43.924 28.752 1.00 0.00 B2
ATOM 1860 CA ALA 272 39.176 42.460 29.853 1.00 77.02 B2
ATOM 1861 N ALA 273 39.485 40.547 31.487 1.00 74.93 B2
ATOM 1862 H ALA 273 40.334 40.963 31.745 1.00 0.00 B2
ATOM 1863 CA ALA 273 39.244 39.241 32.119 1.00 72.64 B2
ATOM 1864 CB ALA 273 39.704 39.279 33.558 1.00 71.92 B2
ATOM 1865 C ALA 273 37.872 38.599 32.118 1.00 71.60 B2
ATOM 1866 O ALA 273 37.806 37.458 31.702 1.00 71.68 B2
ATOM 1867 N GLY 274 36.775 39.282 32.484 1.00 70.20 B2
ATOM 1868 H GLY 274 36.903 40.167 32.874 1.00 0.00 B2
ATOM 1869 CA GLY 274 35.412 38.758 32.425 1.00 66.78 B2
ATOM 1870 C GLY 274 35.050 38.437 30.990 1.00 65.05 B2
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FIG.5AA

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ATOM  1871  O  GLY  274     34.627  37.320  30.709  1.00 66.44      B2
ATOM  1872  N  CYS  275     35.301  39.364  30.048  1.00 62.77      B2
ATOM  1873  H  CYS  275     35.634  40.223  30.357  1.00  0.00      B2
ATOM  1874  CA CYS  275     35.026  39.188  28.611  1.00 59.30      B2
ATOM  1875  C  CYS  275     35.875  38.063  28.054  1.00 55.89      B2
ATOM  1876  O  CYS  275     35.425  37.152  27.351  1.00 54.41      B2
ATOM  1877  CB CYS  275     35.349  40.466  27.827  1.00 61.50      B2
ATOM  1878  SG CYS  275     34.119  40.937  26.577  1.00 66.63      B2
ATOM  1879  N  LEU  276     37.124  38.114  28.506  1.00 52.23      B2
ATOM  1880  H  LEU  276     37.350  38.722  29.233  1.00  0.00      B2
ATOM  1881  CA LEU  276     38.091  37.163  28.066  1.00 48.93      B2
ATOM  1882  CB LEU  276     39.483  37.564  28.542  1.00 45.96      B2
ATOM  1883  CG LEU  276     40.241  38.557  27.670  1.00 43.20      B2
ATOM  1884  CD1 LEU  276     41.599  38.782  28.279  1.00 44.63      B2
ATOM  1885  CD2 LEU  276     40.429  38.033  26.271  1.00 40.55      B2
ATOM  1886  C  LEU  276     37.673  35.833  28.638  1.00 47.84      B2
ATOM  1887  O  LEU  276     37.784  34.803  27.964  1.00 48.51      B2
ATOM  1888  N  ALA  277     37.074  35.840  29.804  1.00 45.56      B2
ATOM  1889  H  ALA  277     36.898  36.662  30.289  1.00  0.00      B2
ATOM  1890  CA ALA  277     36.613  34.605  30.365  1.00 45.77      B2
ATOM  1891  CB ALA  277     36.147  34.810  31.783  1.00 47.87      B2
ATOM  1892  C  ALA  277     35.442  34.111  29.542  1.00 45.03      B2
ATOM  1893  O  ALA  277     35.342  32.926  29.271  1.00 44.20      B2
ATOM  1894  N  GLN  278     34.592  35.000  29.049  1.00 45.13      B2
ATOM  1895  H  GLN  278     34.731  35.944  29.263  1.00  0.00      B2
ATOM  1896  CA GLN  278     33.435  34.601  28.284  1.00 45.27      B2
ATOM  1897  CB GLN  278     32.550  35.825  28.083  1.00 48.13      B2
ATOM  1898  CG GLN  278     31.140  35.442  28.484  1.00 56.00      B2
ATOM  1899  CD GLN  278     30.045  36.464  28.178  1.00 61.94      B2
ATOM  1900  OE1 GLN  278     29.048  36.530  28.896  1.00 65.95      B2
ATOM  1901  NE2 GLN  278     30.080  37.291  27.132  1.00 65.55      B2
ATOM  1902  HE21 GLN  278     30.829  37.221  26.510  1.00  0.00      B2
ATOM  1903  HE22 GLN  278     29.343  37.927  27.056  1.00  0.00      B2
ATOM  1904  C  GLN  278     33.812  33.971  26.950  1.00 43.16      B2
ATOM  1905  O  GLN  278     33.173  33.050  26.462  1.00 40.58      B2
ATOM  1906  N  LEU  279     34.869  34.476  26.331  1.00 43.32      B2
ATOM  1907  H  LEU  279     35.328  35.227  26.767  1.00  0.00      B2
ATOM  1908  CA LEU  279     35.398  33.966  25.069  1.00 42.80      B2
ATOM  1909  CB LEU  279     36.583  34.790  24.626  1.00 41.42      B2
ATOM  1910  CG LEU  279     36.885  35.014  23.190  1.00 40.76      B2
ATOM  1911  CD1 LEU  279     38.239  35.647  23.130  1.00 41.76      B2
ATOM  1912  CD2 LEU  279     36.943  33.753  22.411  1.00 40.01      B2
ATOM  1913  C  LEU  279     35.876  32.554  25.341  1.00 42.92      B2
ATOM  1914  O  LEU  279     35.572  31.598  24.640  1.00 42.57      B2
ATOM  1915  N  HIS  280     36.654  32.463  26.403  1.00 43.93      B2
ATOM  1916  H  HIS  280     36.837  33.282  26.917  1.00  0.00      B2
ATOM  1917  CA HIS  280     37.215  31.223  26.850  1.00 46.12      B2
ATOM  1918  CB HIS  280     38.029  31.506  28.101  1.00 48.74      B2
ATOM  1919  CG HIS  280     38.914  30.320  28.394  1.00 54.16      B2
ATOM  1920  CD2 HIS  280     40.041  30.069  27.650  1.00 56.02      B2
ATOM  1921  ND1 HIS  280     38.759  29.326  29.264  1.00 56.01      B2
ATOM  1922  HD1 HIS  280     38.012  29.203  29.890  1.00  0.00      B2
ATOM  1923  CE1 HIS  280     39.744  28.483  29.058  1.00 56.64      B2
ATOM  1924  NE2 HIS  280     40.507  28.937  28.088  1.00 56.64      B2
ATOM  1925  HE2 HIS  280     41.282  28.478  27.684  1.00  0.00      B2
ATOM  1926  C  HIS  280     36.161  30.134  27.117  1.00 45.65      B2
ATOM  1927  O  HIS  280     36.362  28.977  26.711  1.00 46.23      B2
ATOM  1928  N  SER  281     35.086  30.473  27.822  1.00 43.91      B2
ATOM  1929  H  SER  281     35.009  31.367  28.219  1.00  0.00      B2
ATOM  1930  CA SER  281     34.008  29.574  28.105  1.00 43.53      B2
ATOM  1931  CB SER  281     33.026  30.291  29.002  1.00 44.18      B2
ATOM  1932  OG SER  281     33.761  30.812  30.113  1.00 47.79      B2
ATOM  1933  HG SER  281     33.288  30.648  30.931  1.00  0.00      B2
ATOM  1934  C  SER  281     33.382  29.169  26.787  1.00 43.35      B2
ATOM  1935  O  SER  281     33.334  27.973  26.496  1.00 44.83      B2
ATOM  1936  N  GLY  282     32.977  30.120  25.940  1.00 42.33      B2
ATOM  1937  H  GLY  282     33.043  31.058  26.221  1.00  0.00      B2
ATOM  1938  CA GLY  282     32.363  29.869  24.632  1.00 40.65      B2
ATOM  1939  C  GLY  282     33.175  28.937  23.755  1.00 39.06      B2
ATOM  1940  O  GLY  282     32.584  28.075  23.107  1.00 40.10      B2
ATOM  1941  N  LEU  283     34.514  29.066  23.776  1.00 37.39      B2
ATOM  1942  H  LEU  283     34.880  29.807  24.304  1.00  0.00      B2
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FIG.5BB

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ATOM  1943 CA  LEU  283      35.465  28.213  23.037  1.00 35.06      B2
ATOM  1944 CB  LEU  283      36.902  28.718  23.089  1.00 30.20      B2
ATOM  1945 CG  LEU  283      37.167  30.001  22.302  1.00 25.73      B2
ATOM  1946 CD1 LEU  283      38.539  30.461  22.664  1.00 24.38      B2
ATOM  1947 CD2 LEU  283      37.036  29.802  20.815  1.00 21.94      B2
ATOM  1948 C   LEU  283      35.470  26.851  23.651  1.00 34.81      B2
ATOM  1949 O   LEU  283      35.314  25.859  22.947  1.00 31.09      B2
ATOM  1950 N   PHE  284      35.533  26.842  24.973  1.00 37.62      B2
ATOM  1951 H   PHE  284      35.567  27.686  25.467  1.00  0.00      B2
ATOM  1952 CA  PHE  284      35.485  25.596  25.710  1.00 42.51      B2
ATOM  1953 CB  PHE  284      35.542  25.877  27.184  1.00 49.49      B2
ATOM  1954 CG  PHE  284      36.221  24.770  27.968  1.00 58.39      B2
ATOM  1955 CD1 PHE  284      37.265  25.108  28.816  1.00 63.05      B2
ATOM  1956 CD2 PHE  284      35.810  23.453  27.861  1.00 60.84      B2
ATOM  1957 CE1 PHE  284      37.900  24.124  29.563  1.00 65.86      B2
ATOM  1958 CE2 PHE  284      36.444  22.480  28.605  1.00 64.49      B2
ATOM  1959 CZ  PHE  284      37.486  22.810  29.455  1.00 66.32      B2
ATOM  1960 C   PHE  284      34.204  24.849  25.384  1.00 41.44      B2
ATOM  1961 O   PHE  284      34.257  23.630  25.306  1.00 41.42      B2
ATOM  1962 N   LEU  285      33.100  25.563  25.101  1.00 41.24      B2
ATOM  1963 H   LEU  285      33.192  26.534  25.174  1.00  0.00      B2
ATOM  1964 CA  LEU  285      31.781  25.025  24.730  1.00 38.92      B2
ATOM  1965 CB  LEU  285      30.727  26.139  24.807  1.00 39.05      B2
ATOM  1966 CG  LEU  285      29.292  25.740  24.481  1.00 41.16      B2
ATOM  1967 CD1 LEU  285      28.711  24.981  25.662  1.00 41.12      B2
ATOM  1968 CD2 LEU  285      28.472  26.971  24.139  1.00 39.60      B2
ATOM  1969 C   LEU  285      31.780  24.441  23.329  1.00 37.34      B2
ATOM  1970 O   LEU  285      31.245  23.351  23.095  1.00 36.97      B2
ATOM  1971 N   TYR  286      32.352  25.172  22.372  1.00 35.26      B2
ATOM  1972 H   TYR  286      32.705  26.062  22.593  1.00  0.00      B2
ATOM  1973 CA  TYR  286      32.455  24.660  21.033  1.00 35.04      B2
ATOM  1974 CB  TYR  286      32.891  25.790  20.122  1.00 34.44      B2
ATOM  1975 CG  TYR  286      31.690  26.684  19.808  1.00 34.75      B2
ATOM  1976 CD1 TYR  286      31.433  27.879  20.469  1.00 35.67      B2
ATOM  1977 CE1 TYR  286      30.313  28.620  20.158  1.00 36.90      B2
ATOM  1978 CD2 TYR  286      30.823  26.255  18.839  1.00 36.19      B2
ATOM  1979 CE2 TYR  286      29.707  26.990  18.521  1.00 37.55      B2
ATOM  1980 CZ  TYR  286      29.449  28.164  19.178  1.00 37.73      B2
ATOM  1981 OH  TYR  286      28.285  28.826  18.823  1.00 38.04      B2
ATOM  1982 HH  TYR  286      28.289  29.707  19.243  1.00  0.00      B2
ATOM  1983 C   TYR  286      33.393  23.464  20.926  1.00 34.80      B2
ATOM  1984 O   TYR  286      33.071  22.537  20.180  1.00 35.35      B2
ATOM  1985 N   ALA  287      34.527  23.339  21.636  1.00 34.66      B2
ATOM  1986 H   ALA  287      34.803  24.088  22.206  1.00  0.00      B2
ATOM  1987 CA  ALA  287      35.350  22.108  21.565  1.00 34.28      B2
ATOM  1988 CB  ALA  287      36.617  22.291  22.415  1.00 33.63      B2
ATOM  1989 C   ALA  287      34.528  20.906  22.073  1.00 33.32      B2
ATOM  1990 O   ALA  287      34.535  19.827  21.478  1.00 33.07      B2
ATOM  1991 N   GLY  288      33.723  21.118  23.111  1.00 33.19      B2
ATOM  1992 H   GLY  288      33.791  21.985  23.564  1.00  0.00      B2
ATOM  1993 CA  GLY  288      32.761  20.162  23.655  1.00 35.62      B2
ATOM  1994 C   GLY  288      31.744  19.606  22.636  1.00 36.89      B2
ATOM  1995 O   GLY  288      31.624  18.379  22.444  1.00 34.97      B2
ATOM  1996 N   LEU  289      31.037  20.536  21.966  1.00 36.69      B2
ATOM  1997 H   LEU  289      31.200  21.476  22.201  1.00  0.00      B2
ATOM  1998 CA  LEU  289      30.018  20.249  20.954  1.00 35.05      B2
ATOM  1999 CB  LEU  289      29.351  21.576  20.502  1.00 36.32      B2
ATOM  2000 CG  LEU  289      28.552  22.450  21.464  1.00 35.76      B2
ATOM  2001 CD1 LEU  289      28.256  23.821  20.890  1.00 32.66      B2
ATOM  2002 CD2 LEU  289      27.246  21.780  21.697  1.00 35.35      B2
ATOM  2003 C   LEU  289      30.536  19.519  19.714  1.00 34.21      B2
ATOM  2004 O   LEU  289      29.871  18.694  19.078  1.00 33.28      B2
ATOM  2005 N   LEU  290      31.756  19.902  19.355  1.00 33.25      B2
ATOM  2006 H   LEU  290      32.183  20.634  19.850  1.00  0.00      B2
ATOM  2007 CA  LEU  290      32.448  19.345  18.230  1.00 32.44      B2
ATOM  2008 CB  LEU  290      33.729  20.159  18.000  1.00 32.62      B2
ATOM  2009 CG  LEU  290      33.560  21.509  17.315  1.00 32.05      B2
ATOM  2010 CD1 LEU  290      34.889  22.189  17.349  1.00 32.58      B2
ATOM  2011 CD2 LEU  290      33.068  21.374  15.879  1.00 31.74      B2
ATOM  2012 C   LEU  290      32.737  17.908  18.558  1.00 31.94      B2
ATOM  2013 O   LEU  290      32.432  17.020  17.772  1.00 30.50      B2
ATOM  2014 N   GLN  291      33.249  17.711  19.770  1.00 33.58      B2
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FIG.5CC

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ATOM 2015 H  GLN 291   33.512 18.494 20.298 1.00 0.00  B2
ATOM 2016 CA GLN 291   33.499 16.372 20.311 1.00 36.39 B2
ATOM 2017 CB GLN 291   33.988 16.490 21.702 1.00 36.86 B2
ATOM 2018 CG GLN 291   34.926 15.367 21.950 1.00 39.48 B2
ATOM 2019 CD GLN 291   35.658 15.503 23.252 1.00 40.79 B2
ATOM 2020 OE1 GLN 291  36.457 14.626 23.549 1.00 44.80 B2
ATOM 2021 NE2 GLN 291  35.494 16.535 24.072 1.00 42.59 B2
ATOM 2022 HE21 GLN 291 34.928 17.287 23.817 1.00 0.00  B2
ATOM 2023 HE22 GLN 291 35.910 16.463 24.958 1.00 0.00  B2
ATOM 2024 C  GLN 291   32.233 15.536 20.307 1.00 36.66 B2
ATOM 2025 O  GLN 291   32.220 14.478 19.707 1.00 37.46 B2
ATOM 2026 N  ALA 292   31.143 16.023 20.913 1.00 38.37 B2
ATOM 2027 H  ALA 292   31.255 16.849 21.418 1.00 0.00  B2
ATOM 2028 CA ALA 292   29.778 15.451 20.857 1.00 39.25 B2
ATOM 2029 CB ALA 292   28.818 16.485 21.444 1.00 40.28 B2
ATOM 2030 C  ALA 292   29.215 14.999 19.484 1.00 38.65 B2
ATOM 2031 O  ALA 292   28.411 14.067 19.356 1.00 37.58 B2
ATOM 2032 N  LEU 293   29.614 15.702 18.430 1.00 39.00 B2
ATOM 2033 H  LEU 293   30.149 16.513 18.574 1.00 0.00  B2
ATOM 2034 CA LEU 293   29.265 15.335 17.077 1.00 39.74 B2
ATOM 2035 CB LEU 293   29.662 16.418 16.106 1.00 37.53 B2
ATOM 2036 CG LEU 293   28.969 17.701 16.138 1.00 34.34 B2
ATOM 2037 CD1 LEU 293  29.547 18.582 15.053 1.00 33.88 B2
ATOM 2038 CD2 LEU 293  27.503 17.462 15.918 1.00 35.69 B2
ATOM 2039 C  LEU 293   29.933 14.060 16.596 1.00 40.86 B2
ATOM 2040 O  LEU 293   29.686 13.669 15.449 1.00 40.58 B2
ATOM 2041 N  GLU 294   30.887 13.495 17.365 1.00 42.12 B2
ATOM 2042 H  GLU 294   31.131 13.963 18.190 1.00 0.00  B2
ATOM 2043 CA GLU 294   31.598 12.253 17.076 1.00 42.89 B2
ATOM 2044 CB GLU 294   30.806 10.984 17.485 1.00 48.38 B2
ATOM 2045 CG GLU 294   30.715 10.614 18.972 1.00 56.26 B2
ATOM 2046 CD GLU 294   29.271 10.408 19.486 1.00 63.70 B2
ATOM 2047 OE1 GLU 294  29.058 10.603 20.702 1.00 67.72 B2
ATOM 2048 OE2 GLU 294  28.363 10.074 18.692 1.00 64.81 B2
ATOM 2049 C  GLU 294   31.972 12.068 15.632 1.00 41.53  B2
ATOM 2050 O  GLU 294   31.804 11.007 15.021 1.00 40.29  B2
ATOM 2051 N  GLY 295   32.424 13.203 15.106 1.00 40.93 B2
ATOM 2052 H  GLY 295   32.357 14.033 15.621 1.00 0.00  B2
ATOM 2053 CA GLY 295   32.998 13.236 13.783 1.00 39.95 B2
ATOM 2054 C  GLY 295   32.027 13.230 12.634 1.00 40.60 B2
ATOM 2055 O  GLY 295   32.477 13.216 11.487 1.00 40.96 B2
ATOM 2056 N  ILE 296   30.728 13.296 12.898 1.00 41.18 B2
ATOM 2057 H  ILE 296   30.446 13.210 13.825 1.00 0.00  B2
ATOM 2058 CA ILE 296   29.687 13.306 11.888 1.00 44.02 B2
ATOM 2059 CB ILE 296   29.683 14.580 11.009 1.00 43.49 B2
ATOM 2060 CG2 ILE 296  28.288 14.685 10.421 1.00 40.56 B2
ATOM 2061 CG1 ILE 296  30.047 15.831 11.793 1.00 45.11 B2
ATOM 2062 CD ILE 296   30.039 17.189 11.062 1.00 46.06 B2
ATOM 2063 C  ILE 296   29.820 12.107 10.949 1.00 46.71 B2
ATOM 2064 O  ILE 296   28.918 11.279 11.060 1.00 50.61 B2
ATOM 2065 N  SER 297   30.767 11.875 10.019 1.00 47.21 B2
ATOM 2066 H  SER 297   31.526 12.491 9.936 1.00 0.00  B2
ATOM 2067 CA SER 297   30.810 10.646 9.234 1.00 46.73 B2
ATOM 2068 CB SER 297   30.239 10.884 7.865 1.00 45.48 B2
ATOM 2069 OG SER 297   30.988 11.782 7.072 1.00 46.27 B2
ATOM 2070 HG SER 297   30.321 12.200 6.503 1.00 0.00  B2
ATOM 2071 C  SER 297   32.263 10.269 9.123 1.00 48.72  B2
ATOM 2072 O  SER 297   33.120 11.122 9.391 1.00 50.55 B2
ATOM 2073 N  PRO 298   32.655 9.069 8.697 1.00 49.68  B2
ATOM 2074 CD PRO 298   31.782 7.964 8.334 1.00 50.62 B2
ATOM 2075 CA PRO 298   34.049 8.701 8.458 1.00 50.33 B2
ATOM 2076 CB PRO 298   33.948 7.308 7.856 1.00 51.53 B2
ATOM 2077 CG PRO 298   32.576 7.266 7.231 1.00 50.43 B2
ATOM 2078 C  PRO 298   34.795 9.692 7.579 1.00 50.08  B2
ATOM 2079 O  PRO 298   35.883 10.137 7.930 1.00 50.50 B2
ATOM 2080 N  GLN 299   34.173 10.086 6.469 1.00 50.48 B2
ATOM 2081 H  GLN 299   33.279 9.729 6.296 1.00 0.00  B2
ATOM 2082 CA GLN 299   34.749 11.050 5.550 1.00 51.74 B2
ATOM 2083 CB GLN 299   33.898 11.236 4.301 1.00 54.33 B2
ATOM 2084 CG GLN 299   33.095 10.067 3.725 1.00 58.11 B2
ATOM 2085 CD GLN 299   31.658 10.086 4.259 1.00 61.49 B2
ATOM 2086 OE1 GLN 299  31.160 9.083 4.776 1.00 61.00 B2
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FIG.5DD

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ATOM  2087 NE2 GLN  299      30.942  11.217   4.204  1.00 62.12      B2
ATOM  2088 HE21 GLN  299     31.345  12.012   3.800  1.00  0.00      B2
ATOM  2089 HE22 GLN  299     30.034  11.191   4.566  1.00  0.00      B2
ATOM  2090 C   GLN  299      34.923  12.453   6.160  1.00 51.04      B2
ATOM  2091 O   GLN  299      35.796  13.186   5.718  1.00 53.38      B2
ATOM  2092 N   LEU  300      34.118  12.918   7.120  1.00 48.15      B2
ATOM  2093 H   LEU  300      33.383  12.351   7.437  1.00  0.00      B2
ATOM  2094 CA  LEU  300      34.272  14.220   7.745  1.00 43.32      B2
ATOM  2095 CB  LEU  300      32.856  14.719   8.021  1.00 41.39      B2
ATOM  2096 CG  LEU  300      32.073  15.546   6.974  1.00 37.99      B2
ATOM  2097 CD1 LEU  300      31.872  14.824   5.688  1.00 38.34      B2
ATOM  2098 CD2 LEU  300      30.705  15.809   7.522  1.00 37.67      B2
ATOM  2099 C   LEU  300      35.142  14.220   9.019  1.00 42.84      B2
ATOM  2100 O   LEU  300      35.558  15.278   9.541  1.00 41.56      B2
ATOM  2101 N   GLY  301      35.467  13.016   9.528  1.00 40.83      B2
ATOM  2102 H   GLY  301      35.157  12.221   9.046  1.00  0.00      B2
ATOM  2103 CA  GLY  301      36.199  12.826  10.779  1.00 38.72      B2
ATOM  2104 C   GLY  301      37.500  13.607  10.887  1.00 37.69      B2
ATOM  2105 O   GLY  301      37.665  14.406  11.809  1.00 37.31      B2
ATOM  2106 N   PRO  302      38.468  13.452   9.985  1.00 37.33      B2
ATOM  2107 CD  PRO  302      38.353  12.630   8.790  1.00 37.77      B2
ATOM  2108 CA  PRO  302      39.676  14.281   9.884  1.00 37.60      B2
ATOM  2109 CB  PRO  302      40.256  13.907   8.541  1.00 36.62      B2
ATOM  2110 CG  PRO  302      39.047  13.487   7.745  1.00 37.94      B2
ATOM  2111 C   PRO  302      39.486  15.782  10.033  1.00 37.45      B2
ATOM  2112 O   PRO  302      40.132  16.398  10.901  1.00 38.33      B2
ATOM  2113 N   THR  303      38.547  16.311   9.204  1.00 37.05      B2
ATOM  2114 H   THR  303      38.085  15.727   8.567  1.00  0.00      B2
ATOM  2115 CA  THR  303      38.119  17.705   9.128  1.00 35.81      B2
ATOM  2116 CB  THR  303      36.963  17.770   8.123  1.00 37.26      B2
ATOM  2117 OG1 THR  303      37.416  17.161   6.909  1.00 39.64      B2
ATOM  2118 HG1 THR  303      37.369  17.785   6.178  1.00  0.00      B2
ATOM  2119 CG2 THR  303      36.469  19.204   7.927  1.00 38.55      B2
ATOM  2120 C   THR  303      37.687  18.223  10.506  1.00 34.93      B2
ATOM  2121 O   THR  303      38.085  19.263  11.063  1.00 35.11      B2
ATOM  2122 N   LEU  304      36.928  17.366  11.150  1.00 33.76      B2
ATOM  2123 H   LEU  304      36.672  16.500  10.762  1.00  0.00      B2
ATOM  2124 CA  LEU  304      36.436  17.746  12.418  1.00 31.01      B2
ATOM  2125 CB  LEU  304      35.345  16.803  12.708  1.00 30.31      B2
ATOM  2126 CG  LEU  304      34.234  17.567  13.320  1.00 31.32      B2
ATOM  2127 CD1 LEU  304      33.121  17.626  12.309  1.00 28.87      B2
ATOM  2128 CD2 LEU  304      33.921  16.970  14.692  1.00 34.23      B2
ATOM  2129 C   LEU  304      37.553  17.726  13.421  1.00 31.86      B2
ATOM  2130 O   LEU  304      37.615  18.623  14.259  1.00 34.21      B2
ATOM  2131 N   ASP  305      38.510  16.811  13.326  1.00 30.56      B2
ATOM  2132 H   ASP  305      38.456  16.117  12.635  1.00  0.00      B2
ATOM  2133 CA  ASP  305      39.576  16.797  14.303  1.00 30.72      B2
ATOM  2134 CB  ASP  305      40.504  15.608  14.114  1.00 36.20      B2
ATOM  2135 CG  ASP  305      39.912  14.201  14.288  1.00 40.64      B2
ATOM  2136 OD1 ASP  305      38.976  14.040  15.103  1.00 37.52      B2
ATOM  2137 OD2 ASP  305      40.426  13.304  13.581  1.00 42.39      B2
ATOM  2138 C   ASP  305      40.435  18.034  14.238  1.00 27.56      B2
ATOM  2139 O   ASP  305      40.775  18.575  15.311  1.00 24.61      B2
ATOM  2140 N   THR  306      40.781  18.417  12.979  1.00 24.77      B2
ATOM  2141 H   THR  306      40.469  17.875  12.230  1.00  0.00      B2
ATOM  2142 CA  THR  306      41.553  19.633  12.751  1.00 24.39      B2
ATOM  2143 CB  THR  306      41.665  19.931  11.318  1.00 24.58      B2
ATOM  2144 OG1 THR  306      42.074  18.753  10.665  1.00 25.13      B2
ATOM  2145 HG1 THR  306      41.447  18.029  10.768  1.00  0.00      B2
ATOM  2146 CG2 THR  306      42.690  21.027  11.089  1.00 25.77      B2
ATOM  2147 C   THR  306      40.893  20.844  13.419  1.00 25.24      B2
ATOM  2148 O   THR  306      41.488  21.472  14.296  1.00 27.24      B2
ATOM  2149 N   LEU  307      39.615  21.134  13.139  1.00 25.91      B2
ATOM  2150 H   LEU  307      39.125  20.547  12.520  1.00  0.00      B2
ATOM  2151 CA  LEU  307      38.900  22.228  13.764  1.00 25.53      B2
ATOM  2152 CB  LEU  307      37.571  22.170  13.142  1.00 25.09      B2
ATOM  2153 CG  LEU  307      36.530  23.097  13.588  1.00 27.93      B2
ATOM  2154 CD1 LEU  307      37.008  24.515  13.484  1.00 29.87      B2
ATOM  2155 CD2 LEU  307      35.311  22.846  12.728  1.00 28.93      B2
ATOM  2156 C   LEU  307      38.850  22.214  15.269  1.00 27.09      B2
ATOM  2157 O   LEU  307      38.854  23.253  15.925  1.00 30.03      B2
ATOM  2158 N   GLN  308      38.875  21.044  15.879  1.00 29.09      B2
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FIG.5EE

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ATOM 2159 H  GLN 308  38.883 20.239 15.319 1.00 0.00  B2
ATOM 2160 CA GLN 308  38.824 20.848 17.340 1.00 29.36 B2
ATOM 2161 CB GLN 308  38.379 19.399 17.562 1.00 29.41 B2
ATOM 2162 CG GLN 308  37.862 19.140 18.935 1.00 32.24 B2
ATOM 2163 CD GLN 308  37.586 17.672 19.165 1.00 34.03 B2
ATOM 2164 OE1 GLN 308 36.973 17.023 18.311 1.00 33.48 B2
ATOM 2165 NE2 GLN 308 38.053 17.127 20.299 1.00 31.67 B2
ATOM 2166 HE21 GLN 308 38.547 17.697 20.917 1.00 0.00 B2
ATOM 2167 HE22 GLN 308 37.875 16.174 20.436 1.00 0.00 B2
ATOM 2168 C  GLN 308  40.154 21.138 18.051 1.00 28.94 B2
ATOM 2169 O  GLN 308  40.196 21.796 19.101 1.00 28.44 B2
ATOM 2170 N  LEU 309  41.269 20.671 17.460 1.00 28.78 B2
ATOM 2171 H  LEU 309  41.157 20.120 16.655 1.00 0.00  B2
ATOM 2172 CA LEU 309  42.632 20.923 17.967 1.00 28.56 B2
ATOM 2173 CB LEU 309  43.671 20.154 17.106 1.00 26.54 B2
ATOM 2174 CG LEU 309  43.632 18.636 17.241 1.00 24.98 B2
ATOM 2175 CD1 LEU 309 44.595 17.935 16.353 1.00 24.17 B2
ATOM 2176 CD2 LEU 309 43.992 18.310 18.621 1.00 23.45 B2
ATOM 2177 C  LEU 309  42.893 22.416 17.909 1.00 28.24 B2
ATOM 2178 O  LEU 309  43.370 22.957 18.907 1.00 30.32 B2
ATOM 2179 N  ASP 310  42.548 23.027 16.749 1.00 26.58 B2
ATOM 2180 H  ASP 310  42.296 22.437 16.007 1.00 0.00  B2
ATOM 2181 CA ASP 310  42.495 24.477 16.495 1.00 27.90 B2
ATOM 2182 CB ASP 310  42.025 24.659 15.076 1.00 28.41 B2
ATOM 2183 CG ASP 310  43.162 24.556 14.096 1.00 31.84 B2
ATOM 2184 OD1 ASP 310 42.959 24.766 12.905 1.00 31.54 B2
ATOM 2185 OD2 ASP 310 44.297 24.314 14.514 1.00 37.32 B2
ATOM 2186 C  ASP 310  41.666 25.410 17.422 1.00 27.99  B2
ATOM 2187 O  ASP 310  42.219 26.429 17.876 1.00 27.23  B2
ATOM 2188 N  VAL 311  40.374 25.086 17.725 1.00 26.29  B2
ATOM 2189 H  VAL 311  39.961 24.347 17.225 1.00 0.00  B2
ATOM 2190 CA VAL 311  39.546 25.803 18.706 1.00 24.29 B2
ATOM 2191 CB VAL 311  38.098 25.217 18.869 1.00 21.47 B2
ATOM 2192 CG1 VAL 311 37.341 25.915 19.949 1.00 19.01 B2
ATOM 2193 CG2 VAL 311 37.261 25.488 17.667 1.00 18.56 B2
ATOM 2194 C  VAL 311  40.270 25.638 20.020 1.00 27.21  B2
ATOM 2195 O  VAL 311  40.437 26.647 20.719 1.00 29.71 B2
ATOM 2196 N  ALA 312  40.762 24.428 20.357 1.00 27.97 B2
ATOM 2197 H  ALA 312  40.585 23.674 19.756 1.00 0.00  B2
ATOM 2198 CA ALA 312  41.515 24.157 21.583 1.00 29.24 B2
ATOM 2199 CB ALA 312  41.855 22.688 21.532 1.00 30.53 B2
ATOM 2200 C  ALA 312  42.778 25.026 21.784 1.00 30.06 B2
ATOM 2201 O  ALA 312  43.057 25.508 22.886 1.00 30.04 B2
ATOM 2202 N  ASP 313  43.554 25.286 20.735 1.00 31.33 B2
ATOM 2203 H  ASP 313  43.433 24.730 19.935 1.00 0.00  B2
ATOM 2204 CA ASP 313  44.610 26.275 20.743 1.00 34.22 B2
ATOM 2205 CB ASP 313  45.279 26.512 19.447 1.00 38.87 B2
ATOM 2206 CG ASP 313  46.071 25.404 18.866 1.00 44.55 B2
ATOM 2207 OD1 ASP 313 46.225 25.439 17.636 1.00 48.67 B2
ATOM 2208 OD2 ASP 313 46.521 24.553 19.647 1.00 49.25 B2
ATOM 2209 C  ASP 313  44.187 27.699 21.059 1.00 35.12  B2
ATOM 2210 O  ASP 313  44.807 28.390 21.894 1.00 38.60  B2
ATOM 2211 N  PHE 314  43.192 28.216 20.339 1.00 33.36  B2
ATOM 2212 H  PHE 314  42.784 27.683 19.619 1.00 0.00  B2
ATOM 2213 CA PHE 314  42.715 29.548 20.600 1.00 31.09 B2
ATOM 2214 CB PHE 314  41.572 29.860 19.631 1.00 32.06 B2
ATOM 2215 CG PHE 314  41.074 31.303 19.636 1.00 33.37 B2
ATOM 2216 CD1 PHE 314 39.780 31.568 19.247 1.00 31.81 B2
ATOM 2217 CD2 PHE 314 41.907 32.354 20.021 1.00 35.65 B2
ATOM 2218 CE1 PHE 314 39.318 32.857 19.240 1.00 29.15 B2
ATOM 2219 CE2 PHE 314 41.455 33.648 20.017 1.00 32.48 B2
ATOM 2220 CZ PHE 314  40.154 33.870 19.622 1.00 32.81 B2
ATOM 2221 C  PHE 314  42.282 29.601 22.057 1.00 29.90  B2
ATOM 2222 O  PHE 314  42.658 30.550 22.764 1.00 26.87  B2
ATOM 2223 N  ALA 315  41.686 28.532 22.584 1.00 29.29  B2
ATOM 2224 H  ALA 315  41.448 27.764 22.022 1.00 0.00  B2
ATOM 2225 CA ALA 315  41.300 28.583 23.961 1.00 31.61 B2
ATOM 2226 CB ALA 315  40.632 27.358 24.451 1.00 32.23 B2
ATOM 2227 C  ALA 315  42.482 28.751 24.836 1.00 34.41  B2
ATOM 2228 O  ALA 315  42.361 29.437 25.853 1.00 37.66  B2
ATOM 2229 N  THR 316  43.646 28.250 24.476 1.00 36.16  B2
ATOM 2230 H  THR 316  43.745 27.778 23.625 1.00 0.00  B2
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FIG.5FF

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ATOM 2231 CA THR 316 44.780 28.388 25.374 1.00 37.99 B2
ATOM 2232 CB THR 316 45.795 27.255 25.156 1.00 41.16 B2
ATOM 2233 OG1 THR 316 45.049 26.081 25.521 1.00 45.50 B2
ATOM 2234 HG1 THR 316 44.316 25.900 24.913 1.00 0.00 B2
ATOM 2235 CG2 THR 316 47.152 27.415 25.888 1.00 40.31 B2
ATOM 2236 C THR 316 45.458 29.710 25.177 1.00 38.47 B2
ATOM 2237 O THR 316 45.903 30.189 26.217 1.00 39.63 B2
ATOM 2238 N THR 317 45.620 30.287 23.970 1.00 36.53 B2
ATOM 2239 H THR 317 45.351 29.800 23.164 1.00 0.00 B2
ATOM 2240 CA THR 317 46.092 31.657 23.844 1.00 37.07 B2
ATOM 2241 CB THR 317 45.866 32.098 22.392 1.00 36.01 B2
ATOM 2242 OG1 THR 317 46.752 31.352 21.575 1.00 35.31 B2
ATOM 2243 HG1 THR 317 46.489 30.441 21.389 1.00 0.00 B2
ATOM 2244 CG2 THR 317 46.109 33.566 22.156 1.00 34.30 B2
ATOM 2245 C THR 317 45.338 32.597 24.832 1.00 39.30 B2
ATOM 2246 O THR 317 45.941 33.378 25.583 1.00 40.17 B2
ATOM 2247 N ILE 318 44.003 32.481 24.912 1.00 40.83 B2
ATOM 2248 H ILE 318 43.554 31.819 24.342 1.00 0.00 B2
ATOM 2249 CA ILE 318 43.172 33.317 25.788 1.00 40.75 B2
ATOM 2250 CB ILE 318 41.621 32.979 25.567 1.00 37.17 B2
ATOM 2251 CG2 ILE 318 40.742 33.706 26.545 1.00 34.29 B2
ATOM 2252 CG1 ILE 318 41.216 33.310 24.160 1.00 31.39 B2
ATOM 2253 CD ILE 318 41.626 34.657 23.614 1.00 29.66 B2
ATOM 2254 C ILE 318 43.624 33.019 27.217 1.00 42.43 B2
ATOM 2255 O ILE 318 44.064 33.963 27.856 1.00 42.54 B2
ATOM 2256 N TRP 319 43.662 31.784 27.744 1.00 44.17 B2
ATOM 2257 H TRP 319 43.537 31.008 27.163 1.00 0.00 B2
ATOM 2258 CA TRP 319 43.994 31.633 29.142 1.00 46.90 B2
ATOM 2259 CB TRP 319 43.892 30.179 29.597 1.00 50.64 B2
ATOM 2260 CG TRP 319 43.998 30.094 31.131 1.00 56.05 B2
ATOM 2261 CD2 TRP 319 43.005 30.397 32.038 1.00 58.61 B2
ATOM 2262 CE2 TRP 319 43.685 30.281 33.251 1.00 60.50 B2
ATOM 2263 CE3 TRP 319 41.668 30.740 32.005 1.00 60.12 B2
ATOM 2264 CD1 TRP 319 45.188 29.788 31.760 1.00 58.07 B2
ATOM 2265 NE1 TRP 319 44.968 29.921 33.042 1.00 60.07 B2
ATOM 2266 HE1 TRP 319 45.637 29.765 33.740 1.00 0.00 B2
ATOM 2267 CZ2 TRP 319 43.044 30.512 34.456 1.00 61.00 B2
ATOM 2268 CZ3 TRP 319 41.022 30.967 33.210 1.00 61.58 B2
ATOM 2269 CH2 TRP 319 41.704 30.854 34.417 1.00 62.04 B2
ATOM 2270 C TRP 319 45.398 32.136 29.456 1.00 47.85 B2
ATOM 2271 O TRP 319 45.635 32.772 30.490 1.00 47.99 B2
ATOM 2272 N GLN 320 46.339 31.915 28.550 1.00 48.63 B2
ATOM 2273 H GLN 320 46.091 31.482 27.708 1.00 0.00 B2
ATOM 2274 CA GLN 320 47.706 32.319 28.767 1.00 49.45 B2
ATOM 2275 CB GLN 320 48.567 31.988 27.589 1.00 51.44 B2
ATOM 2276 CG GLN 320 48.828 30.494 27.444 1.00 55.03 B2
ATOM 2277 CD GLN 320 49.958 30.349 26.438 1.00 60.17 B2
ATOM 2278 OE1 GLN 320 51.116 30.465 26.834 1.00 65.26 B2
ATOM 2279 NE2 GLN 320 49.771 30.145 25.131 1.00 59.32 B2
ATOM 2280 HE21 GLN 320 48.859 30.087 24.789 1.00 0.00 B2
ATOM 2281 HE22 GLN 320 50.582 30.083 24.590 1.00 0.00 B2
ATOM 2282 C GLN 320 47.717 33.790 28.983 1.00 49.62 B2
ATOM 2283 O GLN 320 48.251 34.209 29.987 1.00 49.91 B2
ATOM 2284 N GLN 321 46.998 34.538 28.150 1.00 51.76 B2
ATOM 2285 H GLN 321 46.535 34.102 27.403 1.00 0.00 B2
ATOM 2286 CA GLN 321 46.837 35.988 28.278 1.00 52.08 B2
ATOM 2287 CB GLN 321 46.015 36.571 27.151 1.00 49.72 B2
ATOM 2288 CG GLN 321 45.873 38.058 27.166 1.00 51.19 B2
ATOM 2289 CD GLN 321 47.211 38.781 27.201 1.00 53.13 B2
ATOM 2290 OE1 GLN 321 48.090 38.622 26.364 1.00 55.36 B2
ATOM 2291 NE2 GLN 321 47.468 39.618 28.177 1.00 53.21 B2
ATOM 2292 HE21 GLN 321 46.800 39.713 28.889 1.00 0.00 B2
ATOM 2293 HE22 GLN 321 48.338 40.057 28.168 1.00 0.00 B2
ATOM 2294 C GLN 321 46.112 36.315 29.562 1.00 53.30 B2
ATOM 2295 O GLN 321 46.293 37.422 30.058 1.00 54.39 B2
ATOM 2296 N MET 322 45.269 35.441 30.117 1.00 54.50 B2
ATOM 2297 H MET 322 45.098 34.592 29.662 1.00 0.00 B2
ATOM 2298 CA MET 322 44.619 35.748 31.375 1.00 55.42 B2
ATOM 2299 CB MET 322 43.595 34.690 31.713 1.00 52.93 B2
ATOM 2300 CG MET 322 42.527 34.865 30.658 1.00 51.76 B2
ATOM 2301 SD MET 322 40.861 34.428 31.189 1.00 54.19 B2
ATOM 2302 CE MET 322 40.293 33.192 30.069 1.00 52.53 B2
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FIG.5GG

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ATOM 2303 C  MET 322  45.700 35.811 32.432 1.00 57.69  B2
ATOM 2304 O  MET 322  45.781 36.739 33.248 1.00 57.85  B2
ATOM 2305 N  GLU 323  46.652 34.900 32.319 1.00 60.28  B2
ATOM 2306 H  GLU 323  46.637 34.296 31.544 1.00  0.00  B2
ATOM 2307 CA GLU 323  47.741 34.875 33.273 1.00 62.99  B2
ATOM 2308 CB GLU 323  48.558 33.635 32.957 1.00 65.81  B2
ATOM 2309 CG GLU 323  47.640 32.423 32.918 1.00 68.36  B2
ATOM 2310 CD GLU 323  48.303 31.125 33.310 1.00 71.21  B2
ATOM 2311 OE1 GLU 323  47.651 30.364 34.044 1.00 71.19  B2
ATOM 2312 OE2 GLU 323  49.451 30.900 32.884 1.00 72.43  B2
ATOM 2313 C  GLU 323  48.648 36.124 33.418 1.00 63.96  B2
ATOM 2314 OT1 GLU 323  48.782 36.492 34.584 1.00 64.11  B2
ATOM 2315 OT2 GLU 323  49.169 36.725 32.449 1.00 62.96  B2
ATOM 2316 CB MET 338  27.559 17.690 25.056 1.00 62.56  B3
ATOM 2317 CG MET 338  28.087 18.862 24.222 1.00 63.85  B3
ATOM 2318 SD MET 338  28.738 20.224 25.219 1.00 66.95  B3
ATOM 2319 CE MET 338  27.328 21.252 25.515 1.00 65.50  B3
ATOM 2320 C  MET 338  24.988 17.301 25.122 1.00 57.55  B3
ATOM 2321 O  MET 338  24.417 16.347 25.667 1.00 56.47  B3
ATOM 2322 HT1 MET 338  26.255 16.010 26.594 1.00  0.00  B3
ATOM 2323 HT2 MET 338  25.375 17.061 27.500 1.00  0.00  B3
ATOM 2324 N  MET 338  26.286 16.971 27.009 1.00 61.55  B3
ATOM 2325 HT3 MET 338  27.108 17.107 27.620 1.00  0.00  B3
ATOM 2326 CA MET 338  26.226 17.853 25.851 1.00 60.35  B3
ATOM 2327 N  PRO 339  24.493 17.830 23.998 1.00 55.58  B3
ATOM 2328 CD PRO 339  24.914 19.075 23.375 1.00 54.39  B3
ATOM 2329 CA PRO 339  23.453 17.226 23.164 1.00 54.62  B3
ATOM 2330 CB PRO 339  23.463 18.098 21.903 1.00 53.52  B3
ATOM 2331 CG PRO 339  24.845 18.711 21.909 1.00 53.04  B3
ATOM 2332 C  PRO 339  23.666 15.748 22.881 1.00 53.61  B3
ATOM 2333 O  PRO 339  24.730 15.222 23.169 1.00 53.35  B3
ATOM 2334 N  ALA 340  22.704 15.045 22.333 1.00 54.32  B3
ATOM 2335 H  ALA 340  21.844 15.460 22.111 1.00  0.00  B3
ATOM 2336 CA ALA 340  22.909 13.651 21.968 1.00 56.04  B3
ATOM 2337 CB ALA 340  21.867 12.713 22.625 1.00 57.60  B3
ATOM 2338 C  ALA 340  22.617 13.713 20.495 1.00 55.61  B3
ATOM 2339 O  ALA 340  21.426 13.783 20.196 1.00 58.64  B3
ATOM 2340 N  PHE 341  23.516 13.734 19.514 1.00 53.34  B3
ATOM 2341 H  PHE 341  24.472 13.607 19.685 1.00  0.00  B3
ATOM 2342 CA PHE 341  23.016 13.900 18.158 1.00 49.92  B3
ATOM 2343 CB PHE 341  24.050 14.541 17.244 1.00 48.16  B3
ATOM 2344 CG PHE 341  24.382 15.940 17.658 1.00 45.00  B3
ATOM 2345 CD1 PHE 341  23.510 16.923 17.359 1.00 43.44  B3
ATOM 2346 CD2 PHE 341  25.527 16.175 18.388 1.00 47.03  B3
ATOM 2347 CE1 PHE 341  23.812 18.172 17.831 1.00 49.15  B3
ATOM 2348 CE2 PHE 341  25.827 17.426 18.862 1.00 47.86  B3
ATOM 2349 CZ PHE 341  24.952 18.437 18.580 1.00 48.36  B3
ATOM 2350 C  PHE 341  22.684 12.510 17.672 1.00 49.56  B3
ATOM 2351 O  PHE 341  23.309 11.938 16.781 1.00 51.46  B3
ATOM 2352 N  ALA 342  21.625 11.985 18.245 1.00 47.40  B3
ATOM 2353 H  ALA 342  21.026 12.585 18.741 1.00  0.00  B3
ATOM 2354 CA ALA 342  21.167 10.650 17.997 1.00 46.11  B3
ATOM 2355 CB ALA 342  19.874 10.531 18.804 1.00 47.10  B3
ATOM 2356 C  ALA 342  20.962 10.149 16.556 1.00 44.37  B3
ATOM 2357 O  ALA 342  20.138 9.247 16.418 1.00 45.65  B3
ATOM 2358 N  SER 343  21.537 10.573 15.423 1.00 41.37  B3
ATOM 2359 H  SER 343  22.191 11.301 15.428 1.00  0.00  B3
ATOM 2360 CA SER 343  21.274 9.923 14.145 1.00 38.80  B3
ATOM 2361 CB SER 343  19.842 10.138 13.656 1.00 38.79  B3
ATOM 2362 OG SER 343  19.205 11.300 14.182 1.00 37.75  B3
ATOM 2363 HG SER 343  18.963 11.059 15.092 1.00  0.00  B3
ATOM 2364 C  SER 343  22.172 10.467 13.088 1.00 38.22  B3
ATOM 2365 O  SER 343  22.810 11.471 13.382 1.00 38.30  B3
ATOM 2366 N  ALA 344  22.206 9.845 11.888 1.00 36.73  B3
ATOM 2367 H  ALA 344  21.762 8.978 11.805 1.00  0.00  B3
ATOM 2368 CA ALA 344  22.914 10.384 10.715 1.00 38.09  B3
ATOM 2369 CB ALA 344  22.583 9.640 9.422 1.00 36.78  B3
ATOM 2370 C  ALA 344  22.472 11.842 10.496 1.00 37.72  B3
ATOM 2371 O  ALA 344  23.271 12.765 10.676 1.00 38.42  B3
ATOM 2372 N  PHE 345  21.194 12.042 10.163 1.00 36.10  B3
ATOM 2373 H  PHE 345  20.668 11.298 9.811 1.00  0.00  B3
ATOM 2374 CA PHE 345  20.564 13.338 10.195 1.00 34.69  B3
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FIG.5HH

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ATOM 2375 CB PHE 345 19.040 13.254 10.128 1.00 33.24 B3
ATOM 2376 CG PHE 345 18.462 14.656 9.918 1.00 31.72 B3
ATOM 2377 CD1 PHE 345 17.715 15.223 10.905 1.00 26.64 B3
ATOM 2378 CD2 PHE 345 18.767 15.343 8.745 1.00 29.99 B3
ATOM 2379 CE1 PHE 345 17.284 16.503 10.682 1.00 33.56 B3
ATOM 2380 CE2 PHE 345 18.333 16.619 8.537 1.00 30.81 B3
ATOM 2381 CZ PHE 345 17.581 17.201 9.520 1.00 31.44 B3
ATOM 2382 C PHE 345 20.888 14.145 11.458 1.00 35.02 B3
ATOM 2383 O PHE 345 21.246 15.319 11.292 1.00 37.81 B3
ATOM 2384 N GLN 346 20.814 13.688 12.691 1.00 32.53 B3
ATOM 2385 H GLN 346 20.516 12.778 12.894 1.00 0.00 B3
ATOM 2386 CA GLN 346 21.156 14.586 13.758 1.00 33.46 B3
ATOM 2387 CB GLN 346 20.899 13.985 15.061 1.00 33.80 B3
ATOM 2388 CG GLN 346 19.459 14.284 15.174 1.00 35.68 B3
ATOM 2389 CD GLN 346 18.788 13.658 16.344 1.00 38.48 B3
ATOM 2390 OE1 GLN 346 19.358 13.328 17.374 1.00 41.78 B3
ATOM 2391 NE2 GLN 346 17.508 13.463 16.167 1.00 41.08 B3
ATOM 2392 HE21 GLN 346 17.088 13.724 15.323 1.00 0.00 B3
ATOM 2393 HE22 GLN 346 17.026 13.063 16.919 1.00 0.00 B3
ATOM 2394 C GLN 346 22.564 15.051 13.773 1.00 35.73 B3
ATOM 2395 O GLN 346 22.766 16.231 14.051 1.00 38.18 B3
ATOM 2396 N ARG 347 23.507 14.190 13.431 1.00 35.57 B3
ATOM 2397 H ARG 347 23.248 13.289 13.157 1.00 0.00 B3
ATOM 2398 CA ARG 347 24.907 14.538 13.396 1.00 35.95 B3
ATOM 2399 CB ARG 347 25.760 13.236 13.222 1.00 36.20 B3
ATOM 2400 CG ARG 347 26.198 12.549 14.540 1.00 37.41 B3
ATOM 2401 CD ARG 347 26.986 11.246 14.373 1.00 39.70 B3
ATOM 2402 NE ARG 347 26.072 10.167 14.028 1.00 47.18 B3
ATOM 2403 HE ARG 347 25.416 9.893 14.701 1.00 0.00 B3
ATOM 2404 CZ ARG 347 26.071 9.516 12.846 1.00 48.49 B3
ATOM 2405 NH1 ARG 347 26.938 9.802 11.882 1.00 50.22 B3
ATOM 2406 HH11 ARG 347 27.602 10.528 12.031 1.00 0.00 B3
ATOM 2407 HH12 ARG 347 26.905 9.313 11.011 1.00 0.00 B3
ATOM 2408 NH2 ARG 347 25.130 8.608 12.574 1.00 48.46 B3
ATOM 2409 HH21 ARG 347 24.423 8.408 13.252 1.00 0.00 B3
ATOM 2410 HH22 ARG 347 25.126 8.131 11.697 1.00 0.00 B3
ATOM 2411 C ARG 347 25.183 15.544 12.267 1.00 35.54 B3
ATOM 2412 O ARG 347 25.877 16.549 12.445 1.00 36.73 B3
ATOM 2413 N ARG 348 24.611 15.353 11.096 1.00 34.74 B3
ATOM 2414 H ARG 348 24.043 14.559 11.005 1.00 0.00 B3
ATOM 2415 CA ARG 348 24.802 16.225 9.954 1.00 35.24 B3
ATOM 2416 CB ARG 348 24.091 15.623 8.751 1.00 36.76 B3
ATOM 2417 CG ARG 348 24.778 14.303 8.450 1.00 44.22 B3
ATOM 2418 CD ARG 348 24.014 13.379 7.529 1.00 49.23 B3
ATOM 2419 NE ARG 348 24.705 12.090 7.457 1.00 54.27 B3
ATOM 2420 HE ARG 348 25.300 11.836 8.193 1.00 0.00 B3
ATOM 2421 CZ ARG 348 24.557 11.226 6.430 1.00 53.75 B3
ATOM 2422 NH1 ARG 348 23.758 11.479 5.381 1.00 51.85 B3
ATOM 2423 HH11 ARG 348 23.234 12.329 5.339 1.00 0.00 B3
ATOM 2424 HH12 ARG 348 23.680 10.807 4.645 1.00 0.00 B3
ATOM 2425 NH2 ARG 348 25.252 10.083 6.462 1.00 54.51 B3
ATOM 2426 HH21 ARG 348 25.169 9.424 5.714 1.00 0.00 B3
ATOM 2427 HH22 ARG 348 25.860 9.894 7.232 1.00 0.00 B3
ATOM 2428 C ARG 348 24.283 17.629 10.237 1.00 34.80 B3
ATOM 2429 O ARG 348 25.078 18.564 10.219 1.00 35.16 B3
ATOM 2430 N ALA 349 23.008 17.795 10.607 1.00 33.85 B3
ATOM 2431 H ALA 349 22.470 16.984 10.755 1.00 0.00 B3
ATOM 2432 CA ALA 349 22.352 19.083 10.853 1.00 32.96 B3
ATOM 2433 CB ALA 349 20.809 18.894 11.070 1.00 33.36 B3
ATOM 2434 C ALA 349 22.945 19.746 12.083 1.00 31.84 B3
ATOM 2435 O ALA 349 22.981 20.969 12.210 1.00 30.69 B3
ATOM 2436 N GLY 350 23.444 18.954 13.018 1.00 31.30 B3
ATOM 2437 H GLY 350 23.308 17.984 12.976 1.00 0.00 B3
ATOM 2438 CA GLY 350 24.117 19.505 14.181 1.00 31.08 B3
ATOM 2439 C GLY 350 25.462 20.025 13.753 1.00 30.79 B3
ATOM 2440 O GLY 350 25.974 21.010 14.280 1.00 31.38 B3
ATOM 2441 N GLY 351 25.991 19.374 12.731 1.00 30.03 B3
ATOM 2442 H GLY 351 25.546 18.582 12.367 1.00 0.00 B3
ATOM 2443 CA GLY 351 27.263 19.735 12.184 1.00 29.95 B3
ATOM 2444 C GLY 351 27.182 21.097 11.534 1.00 29.25 B3
ATOM 2445 O GLY 351 27.937 21.974 11.919 1.00 28.73 B3
ATOM 2446 N VAL 352 26.336 21.285 10.522 1.00 28.92 B3
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FIG.5II

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ATOM  2447 H   VAL  352      25.859  20.484  10.214  1.00  0.00      B3
ATOM  2448 CA  VAL  352      26.079  22.567   9.881  1.00 28.59      B3
ATOM  2449 CB  VAL  352      24.845  22.452   9.004  1.00 28.96      B3
ATOM  2450 CG1 VAL  352      24.627  23.785   8.346  1.00 30.86      B3
ATOM  2451 CG2 VAL  352      25.021  21.475   7.875  1.00 26.94      B3
ATOM  2452 C   VAL  352      25.849  23.709  10.890  1.00 29.29      B3
ATOM  2453 O   VAL  352      26.520  24.747  10.853  1.00 31.02      B3
ATOM  2454 N   LEU  353      24.923  23.543  11.819  1.00 27.52      B3
ATOM  2455 H   LEU  353      24.404  22.709  11.838  1.00  0.00      B3
ATOM  2456 CA  LEU  353      24.635  24.548  12.817  1.00 26.18      B3
ATOM  2457 CB  LEU  353      23.434  24.113  13.636  1.00 27.87      B3
ATOM  2458 CG  LEU  353      22.098  24.034  12.931  1.00 26.54      B3
ATOM  2459 CD1 LEU  353      21.064  23.617  13.924  1.00 25.49      B3
ATOM  2460 CD2 LEU  353      21.750  25.372  12.320  1.00 28.23      B3
ATOM  2461 C   LEU  353      25.742  24.905  13.772  1.00 27.17      B3
ATOM  2462 O   LEU  353      25.838  26.093  14.088  1.00 28.00      B3
ATOM  2463 N   VAL  354      26.539  23.949  14.318  1.00 27.20      B3
ATOM  2464 H   VAL  354      26.321  23.006  14.139  1.00  0.00      B3
ATOM  2465 CA  VAL  354      27.712  24.212  15.157  1.00 24.62      B3
ATOM  2466 CB  VAL  354      28.236  22.910  15.745  1.00 22.01      B3
ATOM  2467 CG1 VAL  354      29.568  23.089  16.406  1.00 19.82      B3
ATOM  2468 CG2 VAL  354      27.276  22.467  16.802  1.00 23.96      B3
ATOM  2469 C   VAL  354      28.812  24.893  14.332  1.00 25.46      B3
ATOM  2470 O   VAL  354      29.439  25.832  14.798  1.00 26.23      B3
ATOM  2471 N   ALA  355      29.059  24.530  13.089  1.00 26.12      B3
ATOM  2472 H   ALA  355      28.579  23.745  12.744  1.00  0.00      B3
ATOM  2473 CA  ALA  355      30.025  25.180  12.235  1.00 26.54      B3
ATOM  2474 CB  ALA  355      30.034  24.591  10.869  1.00 22.08      B3
ATOM  2475 C   ALA  355      29.533  26.601  12.096  1.00 28.51      B3
ATOM  2476 O   ALA  355      30.315  27.498  12.344  1.00 31.93      B3
ATOM  2477 N   SER  356      28.271  26.884  11.802  1.00 30.30      B3
ATOM  2478 H   SER  356      27.654  26.134  11.665  1.00  0.00      B3
ATOM  2479 CA  SER  356      27.778  28.249  11.625  1.00 31.10      B3
ATOM  2480 CB  SER  356      26.401  28.147  11.016  1.00 35.23      B3
ATOM  2481 OG  SER  356      25.679  29.380  10.905  1.00 43.82      B3
ATOM  2482 HG  SER  356      26.250  30.004  10.429  1.00  0.00      B3
ATOM  2483 C   SER  356      27.763  29.095  12.901  1.00 29.75      B3
ATOM  2484 O   SER  356      28.115  30.289  12.898  1.00 28.35      B3
ATOM  2485 N   HIS  357      27.465  28.464  14.025  1.00 27.82      B3
ATOM  2486 H   HIS  357      27.301  27.498  14.019  1.00  0.00      B3
ATOM  2487 CA  HIS  357      27.434  29.194  15.259  1.00 26.58      B3
ATOM  2488 CB  HIS  357      26.735  28.365  16.305  1.00 25.77      B3
ATOM  2489 CG  HIS  357      25.219  28.360  16.063  1.00 27.67      B3
ATOM  2490 CD2 HIS  357      24.563  28.767  14.915  1.00 28.94      B3
ATOM  2491 ND1 HIS  357      24.277  27.963  16.915  1.00 28.43      B3
ATOM  2492 HD1 HIS  357      24.456  27.622  17.828  1.00  0.00      B3
ATOM  2493 CE1 HIS  357      23.112  28.103  16.337  1.00 28.64      B3
ATOM  2494 NE2 HIS  357      23.298  28.589  15.130  1.00 29.48      B3
ATOM  2495 HE2 HIS  357      22.576  28.801  14.495  1.00  0.00      B3
ATOM  2496 C   HIS  357      28.852  29.506  15.645  1.00 27.93      B3
ATOM  2497 O   HIS  357      29.119  30.606  16.115  1.00 29.15      B3
ATOM  2498 N   LEU  358      29.830  28.637  15.383  1.00 28.33      B3
ATOM  2499 H   LEU  358      29.624  27.761  14.997  1.00  0.00      B3
ATOM  2500 CA  LEU  358      31.211  28.940  15.721  1.00 26.39      B3
ATOM  2501 CB  LEU  358      32.030  27.702  15.547  1.00 21.42      B3
ATOM  2502 CG  LEU  358      33.457  27.878  15.734  1.00 20.42      B3
ATOM  2503 CD1 LEU  358      33.805  28.078  17.165  1.00 16.79      B3
ATOM  2504 CD2 LEU  358      34.075  26.714  15.072  1.00 22.89      B3
ATOM  2505 C   LEU  358      31.721  30.067  14.822  1.00 26.45      B3
ATOM  2506 O   LEU  358      32.372  30.939  15.378  1.00 27.12      B3
ATOM  2507 N   GLN  359      31.460  30.130  13.518  1.00 26.41      B3
ATOM  2508 H   GLN  359      31.048  29.337  13.114  1.00  0.00      B3
ATOM  2509 CA  GLN  359      31.863  31.254  12.671  1.00 29.10      B3
ATOM  2510 CB  GLN  359      31.204  31.209  11.292  1.00 30.49      B3
ATOM  2511 CG  GLN  359      31.395  29.952  10.455  1.00 38.94      B3
ATOM  2512 CD  GLN  359      32.842  29.636  10.091  1.00 42.09      B3
ATOM  2513 OE1 GLN  359      33.774  29.979  10.821  1.00 46.15      B3
ATOM  2514 NE2 GLN  359      33.103  28.987   8.967  1.00 41.34      B3
ATOM  2515 HE21 GLN  359      32.341  28.706   8.412  1.00  0.00      B3
ATOM  2516 HE22 GLN  359      34.039  28.838   8.740  1.00  0.00      B3
ATOM  2517 C   GLN  359      31.512  32.621  13.254  1.00 29.39      B3
ATOM  2518 O   GLN  359      32.427  33.427  13.484  1.00 30.06      B3
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FIG.5JJ

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ATOM  2519  N   SER  360      30.201  32.810  13.528  1.00 28.66      B3
ATOM  2520  H   SER  360      29.595  32.061  13.343  1.00  0.00      B3
ATOM  2521  CA  SER  360      29.570  34.003  14.071  1.00 27.31      B3
ATOM  2522  CB  SER  360      28.121  33.761  14.336  1.00 26.70      B3
ATOM  2523  OG  SER  360      27.493  33.539  13.078  1.00 29.72      B3
ATOM  2524  HG  SER  360      26.637  33.112  13.288  1.00  0.00      B3
ATOM  2525  C   SER  360      30.202  34.387  15.353  1.00 27.15      B3
ATOM  2526  O   SER  360      30.575  35.550  15.498  1.00 26.93      B3
ATOM  2527  N   PHE  361      30.383  33.403  16.246  1.00 25.38      B3
ATOM  2528  H   PHE  361      30.055  32.499  16.040  1.00  0.00      B3
ATOM  2529  CA  PHE  361      31.066  33.626  17.517  1.00 25.20      B3
ATOM  2530  CB  PHE  361      31.092  32.335  18.302  1.00 23.30      B3
ATOM  2531  CG  PHE  361      31.796  32.394  19.655  1.00 23.63      B3
ATOM  2532  CD1 PHE  361      31.127  32.854  20.777  1.00 22.44      B3
ATOM  2533  CD2 PHE  361      33.098  31.931  19.770  1.00 23.35      B3
ATOM  2534  CE1 PHE  361      31.772  32.834  22.000  1.00 22.78      B3
ATOM  2535  CE2 PHE  361      33.719  31.921  21.002  1.00 21.26      B3
ATOM  2536  CZ  PHE  361      33.058  32.368  22.114  1.00 19.54      B3
ATOM  2537  C   PHE  361      32.505  34.143  17.385  1.00 26.56      B3
ATOM  2538  O   PHE  361      32.914  34.979  18.183  1.00 26.76      B3
ATOM  2539  N   LEU  362      33.309  33.645  16.441  1.00 28.17      B3
ATOM  2540  H   LEU  362      32.962  32.921  15.874  1.00  0.00      B3
ATOM  2541  CA  LEU  362      34.679  34.089  16.222  1.00 28.89      B3
ATOM  2542  CB  LEU  362      35.452  33.125  15.338  1.00 28.18      B3
ATOM  2543  CG  LEU  362      35.603  31.656  15.781  1.00 29.61      B3
ATOM  2544  CD1 LEU  362      36.306  30.996  14.633  1.00 31.63      B3
ATOM  2545  CD2 LEU  362      36.374  31.433  17.055  1.00 26.38      B3
ATOM  2546  C   LEU  362      34.692  35.449  15.536  1.00 29.18      B3
ATOM  2547  O   LEU  362      35.649  36.202  15.748  1.00 27.43      B3
ATOM  2548  N   GLU  363      33.664  35.763  14.710  1.00 29.54      B3
ATOM  2549  H   GLU  363      33.009  35.066  14.495  1.00  0.00      B3
ATOM  2550  CA  GLU  363      33.496  37.090  14.145  1.00 30.30      B3
ATOM  2551  CB  GLU  363      32.357  37.147  13.228  1.00 30.90      B3
ATOM  2552  CG  GLU  363      32.763  36.735  11.849  1.00 38.69      B3
ATOM  2553  CD  GLU  363      33.642  37.662  11.013  1.00 42.62      B3
ATOM  2554  OE1 GLU  363      33.896  37.282   9.860  1.00 46.58      B3
ATOM  2555  OE2 GLU  363      34.051  38.734  11.488  1.00 46.47      B3
ATOM  2556  C   GLU  363      33.229  38.098  15.244  1.00 30.19      B3
ATOM  2557  O   GLU  363      33.837  39.167  15.239  1.00 30.26      B3
ATOM  2558  N   VAL  364      32.397  37.726  16.217  1.00 30.04      B3
ATOM  2559  H   VAL  364      31.888  36.898  16.100  1.00  0.00      B3
ATOM  2560  CA  VAL  364      32.178  38.522  17.400  1.00 31.90      B3
ATOM  2561  CB  VAL  364      31.014  38.021  18.269  1.00 31.41      B3
ATOM  2562  CG1 VAL  364      30.860  38.811  19.562  1.00 30.73      B3
ATOM  2563  CG2 VAL  364      29.750  38.200  17.497  1.00 29.96      B3
ATOM  2564  C   VAL  364      33.402  38.493  18.275  1.00 35.89      B3
ATOM  2565  O   VAL  364      33.683  39.535  18.855  1.00 37.54      B3
ATOM  2566  N   SER  365      34.173  37.421  18.477  1.00 38.25      B3
ATOM  2567  H   SER  365      33.971  36.577  18.030  1.00  0.00      B3
ATOM  2568  CA  SER  365      35.337  37.478  19.375  1.00 39.61      B3
ATOM  2569  CB  SER  365      36.041  36.113  19.555  1.00 43.00      B3
ATOM  2570  OG  SER  365      35.201  34.953  19.575  1.00 46.29      B3
ATOM  2571  HG  SER  365      34.270  35.189  19.644  1.00  0.00      B3
ATOM  2572  C   SER  365      36.398  38.418  18.840  1.00 38.21      B3
ATOM  2573  O   SER  365      37.103  38.989  19.662  1.00 36.91      B3
ATOM  2574  N   TYR  366      36.575  38.540  17.514  1.00 38.00      B3
ATOM  2575  H   TYR  366      36.079  37.945  16.910  1.00  0.00      B3
ATOM  2576  CA  TYR  366      37.568  39.463  16.969  1.00 39.85      B3
ATOM  2577  CB  TYR  366      37.776  39.330  15.436  1.00 38.53      B3
ATOM  2578  CG  TYR  366      38.662  40.447  14.879  1.00 38.21      B3
ATOM  2579  CD1 TYR  366      38.104  41.464  14.129  1.00 37.18      B3
ATOM  2580  CE1 TYR  366      38.918  42.495  13.678  1.00 41.77      B3
ATOM  2581  CD2 TYR  366      40.021  40.443  15.182  1.00 40.21      B3
ATOM  2582  CE2 TYR  366      40.849  41.466  14.739  1.00 40.76      B3
ATOM  2583  CZ  TYR  366      40.297  42.504  13.976  1.00 42.82      B3
ATOM  2584  OH  TYR  366      41.151  43.522  13.493  1.00 41.30      B3
ATOM  2585  HH  TYR  366      40.743  43.977  12.755  1.00  0.00      B3
ATOM  2586  C   TYR  366      37.133  40.893  17.241  1.00 40.55      B3
ATOM  2587  O   TYR  366      37.917  41.647  17.798  1.00 40.92      B3
ATOM  2588  N   ARG  367      35.933  41.309  16.853  1.00 41.88      B3
ATOM  2589  H   ARG  367      35.360  40.682  16.360  1.00  0.00      B3
ATOM  2590  CA  ARG  367      35.442  42.653  17.139  1.00 43.32      B3
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FIG.5KK

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ATOM 2591 CB ARG 367 34.013 42.709 16.650 1.00 46.82 B3
ATOM 2592 CG ARG 367 33.528 44.130 16.650 1.00 56.74 B3
ATOM 2593 CD ARG 367 32.069 44.267 16.248 1.00 61.81 B3
ATOM 2594 NE ARG 367 31.723 45.687 16.229 1.00 66.59 B3
ATOM 2595 HE ARG 367 32.438 46.356 16.172 1.00 0.00 B3
ATOM 2596 CZ ARG 367 30.458 46.091 16.308 1.00 69.75 B3
ATOM 2597 NH1 ARG 367 29.448 45.220 16.413 1.00 72.65 B3
ATOM 2598 HH11 ARG 367 29.631 44.236 16.410 1.00 0.00 B3
ATOM 2599 HH12 ARG 367 28.503 45.548 16.445 1.00 0.00 B3
ATOM 2600 NH2 ARG 367 30.160 47.375 16.162 1.00 71.64 B3
ATOM 2601 HH21 ARG 367 29.204 47.665 16.222 1.00 0.00 B3
ATOM 2602 HH22 ARG 367 30.888 48.043 16.013 1.00 0.00 B3
ATOM 2603 C ARG 367 35.551 43.011 18.635 1.00 40.96 B3
ATOM 2604 O ARG 367 35.994 44.090 19.012 1.00 41.10 B3
ATOM 2605 N VAL 368 35.160 42.135 19.542 1.00 39.83 B3
ATOM 2606 H VAL 368 34.726 41.316 19.217 1.00 0.00 B3
ATOM 2607 CA VAL 368 35.331 42.292 20.968 1.00 37.33 B3
ATOM 2608 CB VAL 368 34.748 41.043 21.664 1.00 35.75 B3
ATOM 2609 CG1 VAL 368 35.087 40.867 23.140 1.00 35.10 B3
ATOM 2610 CG2 VAL 368 33.259 41.230 21.586 1.00 33.28 B3
ATOM 2611 C VAL 368 36.813 42.459 21.223 1.00 38.75 B3
ATOM 2612 O VAL 368 37.144 43.498 21.772 1.00 40.11 B3
ATOM 2613 N LEU 369 37.759 41.600 20.835 1.00 39.59 B3
ATOM 2614 H LEU 369 37.492 40.818 20.308 1.00 0.00 B3
ATOM 2615 CA LEU 369 39.180 41.780 21.148 1.00 40.05 B3
ATOM 2616 CB LEU 369 39.984 40.601 20.679 1.00 37.15 B3
ATOM 2617 CG LEU 369 39.831 39.335 21.426 1.00 37.54 B3
ATOM 2618 CD1 LEU 369 40.349 38.238 20.528 1.00 39.70 B3
ATOM 2619 CD2 LEU 369 40.563 39.394 22.747 1.00 36.86 B3
ATOM 2620 C LEU 369 39.817 43.031 20.542 1.00 41.88 B3
ATOM 2621 O LEU 369 40.711 43.654 21.144 1.00 41.30 B3
ATOM 2622 N ARG 370 39.333 43.413 19.354 1.00 42.80 B3
ATOM 2623 H ARG 370 38.619 42.884 18.957 1.00 0.00 B3
ATOM 2624 CA ARG 370 39.819 44.577 18.663 1.00 44.96 B3
ATOM 2625 CB ARG 370 39.184 44.569 17.316 1.00 42.06 B3
ATOM 2626 CG ARG 370 39.424 45.719 16.371 1.00 43.93 B3
ATOM 2627 CD ARG 370 40.894 45.910 16.169 1.00 45.37 B3
ATOM 2628 NE ARG 370 41.219 46.681 14.976 1.00 48.00 B3
ATOM 2629 HE ARG 370 40.524 46.867 14.312 1.00 0.00 B3
ATOM 2630 CZ ARG 370 42.469 47.153 14.791 1.00 48.45 B3
ATOM 2631 NH1 ARG 370 43.443 46.961 15.691 1.00 49.13 B3
ATOM 2632 HH11 ARG 370 43.262 46.456 16.534 1.00 0.00 B3
ATOM 2633 HH12 ARG 370 44.357 47.326 15.520 1.00 0.00 B3
ATOM 2634 NH2 ARG 370 42.821 47.710 13.635 1.00 47.59 B3
ATOM 2635 HH21 ARG 370 42.163 47.785 12.889 1.00 0.00 B3
ATOM 2636 HH22 ARG 370 43.751 48.057 13.516 1.00 0.00 B3
ATOM 2637 C ARG 370 39.386 45.740 19.558 1.00 49.12 B3
ATOM 2638 O ARG 370 40.216 46.615 19.826 1.00 49.67 B3
ATOM 2639 N HIS 371 38.162 45.728 20.123 1.00 52.30 B3
ATOM 2640 H HIS 371 37.581 44.955 19.949 1.00 0.00 B3
ATOM 2641 CA HIS 371 37.745 46.738 21.080 1.00 56.65 B3
ATOM 2642 CB HIS 371 36.284 46.604 21.459 1.00 62.15 B3
ATOM 2643 CG HIS 371 35.320 46.991 20.346 1.00 71.70 B3
ATOM 2644 CD2 HIS 371 35.596 47.877 19.313 1.00 75.03 B3
ATOM 2645 ND1 HIS 371 34.067 46.546 20.166 1.00 75.91 B3
ATOM 2646 HD1 HIS 371 33.594 45.897 20.732 1.00 0.00 B3
ATOM 2647 CE1 HIS 371 33.580 47.116 19.077 1.00 77.30 B3
ATOM 2648 NE2 HIS 371 34.507 47.914 18.573 1.00 77.52 B3
ATOM 2649 HE2 HIS 371 34.401 48.460 17.764 1.00 0.00 B3
ATOM 2650 C HIS 371 38.533 46.669 22.382 1.00 56.97 B3
ATOM 2651 O HIS 371 38.458 47.592 23.176 1.00 58.12 B3
ATOM 2652 N LEU 372 39.271 45.632 22.715 1.00 56.98 B3
ATOM 2653 H LEU 372 39.302 44.855 22.122 1.00 0.00 B3
ATOM 2654 CA LEU 372 40.048 45.597 23.939 1.00 57.77 B3
ATOM 2655 CB LEU 372 39.725 44.272 24.633 1.00 57.29 B3
ATOM 2656 CG LEU 372 38.566 44.144 25.611 1.00 55.87 B3
ATOM 2657 CD1 LEU 372 37.358 44.892 25.123 1.00 55.77 B3
ATOM 2658 CD2 LEU 372 38.211 42.675 25.749 1.00 55.33 B3
ATOM 2659 C LEU 372 41.554 45.755 23.647 1.00 58.81 B3
ATOM 2660 O LEU 372 42.447 45.475 24.476 1.00 59.12 B3
ATOM 2661 N ALA 373 41.942 46.168 22.447 1.00 59.27 B3
ATOM 2662 H ALA 373 41.271 46.255 21.731 1.00 0.00 B3
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FIG.5LL

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ATOM 2663 CA ALA 373 43.336 46.425 22.147 1.00 60.03 B3
ATOM 2664 CB ALA 373 43.755 45.485 21.021 1.00 59.87 B3
ATOM 2665 C ALA 373 43.616 47.895 21.762 1.00 61.22 B3
ATOM 2666 OT1 ALA 373 44.798 48.243 21.697 1.00 62.45 B3
ATOM 2667 OT2 ALA 373 42.682 48.700 21.583 1.00 61.55 B3
ATOM 2668 CB LEU 410 23.866 49.243 1.118 1.00 53.10 C1
ATOM 2669 CG LEU 410 23.982 47.812 0.738 1.00 51.85 C1
ATOM 2670 CD1 LEU 410 25.074 47.596 -0.330 1.00 52.64 C1
ATOM 2671 CD2 LEU 410 24.125 47.081 2.058 1.00 49.28 C1
ATOM 2672 C LEU 410 22.381 51.214 1.635 1.00 52.99 C1
ATOM 2673 O LEU 410 22.242 52.166 0.845 1.00 53.00 C1
ATOM 2674 HT1 LEU 410 22.721 50.836 -0.665 1.00 0.00 C1
ATOM 2675 HT2 LEU 410 21.194 50.178 -0.557 1.00 0.00 C1
ATOM 2676 N LEU 410 22.198 49.968 -0.415 1.00 54.31 C1
ATOM 2677 HT3 LEU 410 22.529 49.174 -0.998 1.00 0.00 C1
ATOM 2678 CA LEU 410 22.478 49.815 1.004 1.00 53.64 C1
ATOM 2679 N PRO 411 22.450 51.433 2.965 1.00 52.95 C1
ATOM 2680 CD PRO 411 22.466 50.407 4.022 1.00 52.54 C1
ATOM 2681 CA PRO 411 22.666 52.766 3.548 1.00 53.25 C1
ATOM 2682 CB PRO 411 22.688 52.541 5.068 1.00 52.85 C1
ATOM 2683 CG PRO 411 23.163 51.108 5.203 1.00 52.83 C1
ATOM 2684 C PRO 411 23.958 53.413 3.023 1.00 53.47 C1
ATOM 2685 O PRO 411 25.073 52.878 3.167 1.00 54.02 C1
ATOM 2686 N GLN 412 23.787 54.599 2.411 1.00 52.79 C1
ATOM 2687 H GLN 412 22.863 54.900 2.294 1.00 0.00 C1
ATOM 2688 CA GLN 412 24.873 55.413 1.871 1.00 50.44 C1
ATOM 2689 CB GLN 412 24.387 56.762 1.413 1.00 52.47 C1
ATOM 2690 CG GLN 412 25.364 57.408 0.437 1.00 56.51 C1
ATOM 2691 CD GLN 412 25.228 56.954 -1.017 1.00 59.40 C1
ATOM 2692 OE1 GLN 412 25.869 57.506 -1.913 1.00 59.67 C1
ATOM 2693 NE2 GLN 412 24.336 56.022 -1.389 1.00 60.12 C1
ATOM 2694 HE21 GLN 412 23.734 55.616 -0.737 1.00 0.00 C1
ATOM 2695 HE22 GLN 412 24.396 55.748 -2.328 1.00 0.00 C1
ATOM 2696 C GLN 412 25.930 55.646 2.916 1.00 48.22 C1
ATOM 2697 O GLN 412 27.089 55.591 2.545 1.00 46.78 C1
ATOM 2698 N SER 413 25.614 55.842 4.201 1.00 47.90 C1
ATOM 2699 H SER 413 24.693 55.976 4.492 1.00 0.00 C1
ATOM 2700 CA SER 413 26.696 55.984 5.144 1.00 48.75 C1
ATOM 2701 CB SER 413 26.261 56.344 6.548 1.00 50.61 C1
ATOM 2702 OG SER 413 27.378 56.872 7.301 1.00 53.05 C1
ATOM 2703 HG SER 413 28.178 56.355 7.145 1.00 0.00 C1
ATOM 2704 C SER 413 27.480 54.684 5.267 1.00 48.71 C1
ATOM 2705 O SER 413 28.698 54.839 5.392 1.00 50.77 C1
ATOM 2706 N PHE 414 26.947 53.440 5.208 1.00 46.01 C1
ATOM 2707 H PHE 414 25.996 53.323 5.015 1.00 0.00 C1
ATOM 2708 CA PHE 414 27.787 52.233 5.274 1.00 42.92 C1
ATOM 2709 CB PHE 414 26.959 50.915 5.232 1.00 40.76 C1
ATOM 2710 CG PHE 414 27.633 49.627 4.757 1.00 35.06 C1
ATOM 2711 CD1 PHE 414 27.583 49.256 3.425 1.00 34.71 C1
ATOM 2712 CD2 PHE 414 28.262 48.800 5.663 1.00 34.81 C1
ATOM 2713 CE1 PHE 414 28.156 48.056 3.014 1.00 36.16 C1
ATOM 2714 CE2 PHE 414 28.832 47.602 5.247 1.00 33.40 C1
ATOM 2715 CZ PHE 414 28.781 47.223 3.923 1.00 34.22 C1
ATOM 2716 C PHE 414 28.667 52.271 4.044 1.00 41.25 C1
ATOM 2717 O PHE 414 29.831 51.902 4.110 1.00 41.47 C1
ATOM 2718 N LEU 415 28.122 52.748 2.942 1.00 39.50 C1
ATOM 2719 H LEU 415 27.188 53.044 2.946 1.00 0.00 C1
ATOM 2720 CA LEU 415 28.865 52.769 1.721 1.00 39.91 C1
ATOM 2721 CB LEU 415 27.946 53.205 0.641 1.00 41.98 C1
ATOM 2722 CG LEU 415 27.903 52.274 -0.526 1.00 44.75 C1
ATOM 2723 CD1 LEU 415 26.430 51.951 -0.780 1.00 42.93 C1
ATOM 2724 CD2 LEU 415 28.793 52.853 -1.648 1.00 45.91 C1
ATOM 2725 C LEU 415 30.081 53.669 1.755 1.00 40.03 C1
ATOM 2726 O LEU 415 31.142 53.348 1.183 1.00 40.28 C1
ATOM 2727 N LEU 416 29.901 54.779 2.487 1.00 37.46 C1
ATOM 2728 H LEU 416 29.028 54.948 2.899 1.00 0.00 C1
ATOM 2729 CA LEU 416 30.942 55.756 2.602 1.00 34.05 C1
ATOM 2730 CB LEU 416 30.294 57.089 2.998 1.00 34.67 C1
ATOM 2731 CG LEU 416 29.438 57.704 1.851 1.00 35.24 C1
ATOM 2732 CD1 LEU 416 28.770 58.948 2.358 1.00 31.87 C1
ATOM 2733 CD2 LEU 416 30.310 57.948 0.593 1.00 35.50 C1
ATOM 2734 C LEU 416 31.952 55.258 3.586 1.00 31.97 C1
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FIG.5MM

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ATOM 2735 O  LEU 416      33.131 55.427  3.270 1.00 33.32      C1
ATOM 2736 N  ALA 417      31.573 54.619  4.695 1.00 29.05      C1
ATOM 2737 H  ALA 417      30.621 54.616  4.927 1.00  0.00      C1
ATOM 2738 CA ALA 417      32.524 53.882  5.561 1.00 29.64      C1
ATOM 2739 CB ALA 417      31.853 53.087  6.680 1.00 25.16      C1
ATOM 2740 C  ALA 417      33.319 52.827  4.777 1.00 30.68      C1
ATOM 2741 O  ALA 417      34.536 52.721  4.877 1.00 31.52      C1
ATOM 2742 N  CYS 418      32.726 52.041  3.905 1.00 32.19      C1
ATOM 2743 H  CYS 418      31.748 52.017  3.860 1.00  0.00      C1
ATOM 2744 CA CYS 418      33.499 51.119  3.103 1.00 33.67      C1
ATOM 2745 CB CYS 418      32.657 50.250  2.226 1.00 33.85      C1
ATOM 2746 SG CYS 418      31.623 49.208  3.246 1.00 37.80      C1
ATOM 2747 C  CYS 418      34.446 51.818  2.170 1.00 34.80      C1
ATOM 2748 O  CYS 418      35.626 51.441  2.173 1.00 36.47      C1
ATOM 2749 N  LEU 419      34.009 52.820  1.377 1.00 35.00      C1
ATOM 2750 H  LEU 419      33.082 53.131  1.460 1.00  0.00      C1
ATOM 2751 CA LEU 419      34.886 53.446  0.375 1.00 34.14      C1
ATOM 2752 CB LEU 419      34.062 54.484 -0.413 1.00 37.09      C1
ATOM 2753 CG LEU 419      32.866 53.853 -1.244 1.00 39.61      C1
ATOM 2754 CD1 LEU 419     31.866 54.918 -1.609 1.00 39.24      C1
ATOM 2755 CD2 LEU 419     33.349 53.207 -2.553 1.00 40.02      C1
ATOM 2756 C  LEU 419      36.102 54.041  1.047 1.00 32.33      C1
ATOM 2757 O  LEU 419      37.198 53.973  0.549 1.00 31.60      C1
ATOM 2758 N  GLU 420      35.974 54.483  2.273 1.00 31.92      C1
ATOM 2759 H  GLU 420      35.068 54.528  2.648 1.00  0.00      C1
ATOM 2760 CA GLU 420      37.078 54.905  3.092 1.00 31.79      C1
ATOM 2761 CB GLU 420      36.477 55.462  4.344 1.00 34.29      C1
ATOM 2762 CG GLU 420      37.430 56.240  5.185 1.00 38.66      C1
ATOM 2763 CD GLU 420      36.952 56.499  6.609 1.00 45.20      C1
ATOM 2764 OE1 GLU 420     37.873 56.849  7.367 1.00 45.67      C1
ATOM 2765 OE2 GLU 420     35.745 56.345  6.954 1.00 44.21      C1
ATOM 2766 C  GLU 420      38.043 53.763  3.423 1.00 31.87      C1
ATOM 2767 O  GLU 420      39.253 53.949  3.270 1.00 32.82      C1
ATOM 2768 N  GLN 421      37.553 52.624  3.954 1.00 30.46      C1
ATOM 2769 H  GLN 421      36.583 52.556  4.098 1.00  0.00      C1
ATOM 2770 CA GLN 421      38.366 51.461  4.283 1.00 29.34      C1
ATOM 2771 CB GLN 421      37.545 50.389  4.984 1.00 30.88      C1
ATOM 2772 CG GLN 421      37.308 50.634  6.463 1.00 33.58      C1
ATOM 2773 CD GLN 421      36.320 49.625  7.058 1.00 37.89      C1
ATOM 2774 OE1 GLN 421     35.357 49.236  6.398 1.00 43.18      C1
ATOM 2775 NE2 GLN 421     36.427 49.095  8.275 1.00 37.13      C1
ATOM 2776 HE21 GLN 421    35.695 48.505  8.556 1.00  0.00      C1
ATOM 2777 HE22 GLN 421    37.207 49.330  8.812 1.00  0.00      C1
ATOM 2778 C  GLN 421      38.991 50.862  3.026 1.00 27.36      C1
ATOM 2779 O  GLN 421      40.152 50.445  3.099 1.00 29.09      C1
ATOM 2780 N  VAL 422      38.379 50.845  1.847 1.00 23.57      C1
ATOM 2781 H  VAL 422      37.448 51.138  1.803 1.00  0.00      C1
ATOM 2782 CA VAL 422      39.077 50.420  0.651 1.00 23.52      C1
ATOM 2783 CB VAL 422      38.163 50.636 -0.556 1.00 22.67      C1
ATOM 2784 CG1 VAL 422     38.873 50.455 -1.868 1.00 21.56      C1
ATOM 2785 CG2 VAL 422     37.057 49.610 -0.465 1.00 26.79      C1
ATOM 2786 C  VAL 422      40.353 51.254  0.514 1.00 26.22      C1
ATOM 2787 O  VAL 422      41.458 50.708  0.508 1.00 28.77      C1
ATOM 2788 N  ARG 423      40.275 52.599  0.575 1.00 27.49      C1
ATOM 2789 H  ARG 423      39.402 53.016  0.735 1.00  0.00      C1
ATOM 2790 CA ARG 423      41.436 53.456  0.346 1.00 25.91      C1
ATOM 2791 CB ARG 423      41.098 54.943  0.312 1.00 24.39      C1
ATOM 2792 CG ARG 423      40.167 55.366 -0.807 1.00 22.81      C1
ATOM 2793 CD ARG 423      40.525 54.798 -2.172 1.00 25.55      C1
ATOM 2794 NE ARG 423      39.707 55.387 -3.216 1.00 25.38      C1
ATOM 2795 HE ARG 423      39.168 56.173 -2.989 1.00  0.00      C1
ATOM 2796 CZ ARG 423      39.629 54.928 -4.466 1.00 27.32      C1
ATOM 2797 NH1 ARG 423     40.264 53.857 -4.949 1.00 26.37      C1
ATOM 2798 HH11 ARG 423    40.884 53.341 -4.365 1.00  0.00      C1
ATOM 2799 HH12 ARG 423    40.150 53.595 -5.907 1.00  0.00      C1
ATOM 2800 NH2 ARG 423     38.960 55.682 -5.325 1.00 30.38      C1
ATOM 2801 HH21 ARG 423    38.539 56.537 -5.023 1.00  0.00      C1
ATOM 2802 HH22 ARG 423    38.865 55.385 -6.275 1.00  0.00      C1
ATOM 2803 C  ARG 423      42.429 53.241  1.432 1.00 23.60      C1
ATOM 2804 O  ARG 423      43.594 53.147  1.127 1.00 24.37      C1
ATOM 2805 N  LYS 424      42.065 53.050  2.668 1.00 24.38      C1
ATOM 2806 H  LYS 424      41.109 53.051  2.890 1.00  0.00      C1
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FIG.5NN

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ATOM  2807 CA  LYS  424      43.043  52.855   3.722  1.00 25.12      C1
ATOM  2808 CB  LYS  424      42.352  52.791   5.051  1.00 23.89      C1
ATOM  2809 CG  LYS  424      43.312  52.936   6.190  1.00 28.56      C1
ATOM  2810 CD  LYS  424      42.579  52.580   7.486  1.00 35.51      C1
ATOM  2811 CE  LYS  424      41.338  53.425   7.853  1.00 40.33      C1
ATOM  2812 NZ  LYS  424      40.519  52.722   8.834  1.00 42.23      C1
ATOM  2813 HZ1 LYS  424      41.079  52.559   9.695  1.00  0.00      C1
ATOM  2814 HZ2 LYS  424      40.208  51.814   8.435  1.00  0.00      C1
ATOM  2815 HZ3 LYS  424      39.689  53.306   9.065  1.00  0.00      C1
ATOM  2816 C   LYS  424      43.761  51.547   3.462  1.00 27.10      C1
ATOM  2817 O   LYS  424      44.923  51.425   3.848  1.00 30.64      C1
ATOM  2818 N   ILE  425      43.190  50.542   2.794  1.00 26.83      C1
ATOM  2819 H   ILE  425      42.260  50.607   2.488  1.00  0.00      C1
ATOM  2820 CA  ILE  425      43.949  49.312   2.561  1.00 25.46      C1
ATOM  2821 CB  ILE  425      42.965  48.093   2.336  1.00 24.91      C1
ATOM  2822 CG2 ILE  425      43.654  46.786   1.995  1.00 22.01      C1
ATOM  2823 CG1 ILE  425      42.229  47.909   3.633  1.00 25.34      C1
ATOM  2824 CD  ILE  425      40.885  47.169   3.432  1.00 25.68      C1
ATOM  2825 C   ILE  425      44.824  49.549   1.346  1.00 23.84      C1
ATOM  2826 O   ILE  425      45.959  49.069   1.316  1.00 24.57      C1
ATOM  2827 N   GLN  426      44.361  50.267   0.323  1.00 23.28      C1
ATOM  2828 H   GLN  426      43.451  50.630   0.393  1.00  0.00      C1
ATOM  2829 CA  GLN  426      45.164  50.531  -0.871  1.00 24.13      C1
ATOM  2830 CB  GLN  426      44.421  51.344  -1.896  1.00 24.04      C1
ATOM  2831 CG  GLN  426      43.275  50.539  -2.396  1.00 23.56      C1
ATOM  2832 CD  GLN  426      42.446  51.105  -3.511  1.00 23.92      C1
ATOM  2833 OE1 GLN  426      41.704  52.047  -3.345  1.00 25.34      C1
ATOM  2834 NE2 GLN  426      42.337  50.509  -4.672  1.00 27.55      C1
ATOM  2835 HE21 GLN  426      41.755  50.948  -5.323  1.00  0.00      C1
ATOM  2836 HE22 GLN  426      42.850  49.696  -4.851  1.00  0.00      C1
ATOM  2837 C   GLN  426      46.404  51.312  -0.488  1.00 26.69      C1
ATOM  2838 O   GLN  426      47.486  51.109  -1.046  1.00 29.73      C1
ATOM  2839 N   GLY  427      46.300  52.204   0.499  1.00 26.49      C1
ATOM  2840 H   GLY  427      45.410  52.414   0.854  1.00  0.00      C1
ATOM  2841 CA  GLY  427      47.446  52.894   1.022  1.00 24.25      C1
ATOM  2842 C   GLY  427      48.467  51.913   1.589  1.00 23.08      C1
ATOM  2843 O   GLY  427      49.597  51.921   1.106  1.00 22.28      C1
ATOM  2844 N   ASP  428      48.107  51.073   2.575  1.00 22.75      C1
ATOM  2845 H   ASP  428      47.189  51.111   2.918  1.00  0.00      C1
ATOM  2846 CA  ASP  428      49.039  50.108   3.131  1.00 23.87      C1
ATOM  2847 CB  ASP  428      48.415  49.199   4.117  1.00 26.52      C1
ATOM  2848 CG  ASP  428      47.437  49.779   5.097  1.00 28.84      C1
ATOM  2849 OD1 ASP  428      46.420  49.151   5.265  1.00 31.81      C1
ATOM  2850 OD2 ASP  428      47.662  50.804   5.716  1.00 30.77      C1
ATOM  2851 C   ASP  428      49.626  49.191   2.063  1.00 24.16      C1
ATOM  2852 O   ASP  428      50.812  48.896   2.088  1.00 26.17      C1
ATOM  2853 N   GLY  429      48.840  48.822   1.069  1.00 23.01      C1
ATOM  2854 H   GLY  429      47.905  49.113   1.071  1.00  0.00      C1
ATOM  2855 CA  GLY  429      49.289  47.964   0.029  1.00 25.44      C1
ATOM  2856 C   GLY  429      50.405  48.649  -0.716  1.00 27.39      C1
ATOM  2857 O   GLY  429      51.528  48.135  -0.741  1.00 28.51      C1
ATOM  2858 N   ALA  430      50.127  49.840  -1.271  1.00 28.26      C1
ATOM  2859 H   ALA  430      49.216  50.185  -1.172  1.00  0.00      C1
ATOM  2860 CA  ALA  430      51.094  50.643  -2.015  1.00 26.04      C1
ATOM  2861 CB  ALA  430      50.490  51.976  -2.407  1.00 27.93      C1
ATOM  2862 C   ALA  430      52.300  50.927  -1.133  1.00 25.19      C1
ATOM  2863 O   ALA  430      53.393  51.053  -1.655  1.00 25.43      C1
ATOM  2864 N   ALA  431      52.171  50.979   0.186  1.00 24.05      C1
ATOM  2865 H   ALA  431      51.279  50.872   0.579  1.00  0.00      C1
ATOM  2866 CA  ALA  431      53.295  51.213   1.035  1.00 26.29      C1
ATOM  2867 CB  ALA  431      52.874  51.522   2.458  1.00 24.14      C1
ATOM  2868 C   ALA  431      54.139  49.972   1.073  1.00 29.82      C1
ATOM  2869 O   ALA  431      55.360  50.085   0.959  1.00 31.97      C1
ATOM  2870 N   LEU  432      53.562  48.777   1.203  1.00 31.87      C1
ATOM  2871 H   LEU  432      52.585  48.726   1.279  1.00  0.00      C1
ATOM  2872 CA  LEU  432      54.337  47.540   1.165  1.00 33.92      C1
ATOM  2873 CB  LEU  432      53.430  46.315   1.301  1.00 37.42      C1
ATOM  2874 CG  LEU  432      54.063  44.952   1.574  1.00 37.40      C1
ATOM  2875 CD1 LEU  432      54.751  44.949   2.950  1.00 38.10      C1
ATOM  2876 CD2 LEU  432      52.966  43.901   1.492  1.00 36.27      C1
ATOM  2877 C   LEU  432      55.096  47.404  -0.146  1.00 33.74      C1
ATOM  2878 O   LEU  432      56.306  47.179  -0.138  1.00 33.29      C1
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FIG.500

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ATOM 2879 N  GLN 433      54.402 47.564 -1.276 1.00 34.57      C1
ATOM 2880 H  GLN 433      53.439 47.733 -1.186 1.00  0.00      C1
ATOM 2881 CA GLN 433      55.002 47.526 -2.600 1.00 35.83      C1
ATOM 2882 CB GLN 433      53.999 47.892 -3.664 1.00 35.52      C1
ATOM 2883 CG GLN 433      52.996 46.823 -3.832 1.00 39.40      C1
ATOM 2884 CD GLN 433      52.049 47.097 -4.973 1.00 42.46      C1
ATOM 2885 OE1 GLN 433     50.924 47.526 -4.786 1.00 48.22      C1
ATOM 2886 NE2 GLN 433     52.376 46.878 -6.225 1.00 44.77      C1
ATOM 2887 HE21 GLN 433    53.271 46.540 -6.433 1.00  0.00      C1
ATOM 2888 HE22 GLN 433    51.693 47.087 -6.892 1.00  0.00      C1
ATOM 2889 C  GLN 433      56.177 48.485 -2.757 1.00 36.48      C1
ATOM 2890 O  GLN 433      57.214 48.118 -3.312 1.00 38.08      C1
ATOM 2891 N  GLU 434      56.055 49.719 -2.287 1.00 36.11      C1
ATOM 2892 H  GLU 434      55.210 49.978 -1.854 1.00  0.00      C1
ATOM 2893 CA GLU 434      57.089 50.719 -2.426 1.00 35.93      C1
ATOM 2894 CB GLU 434      56.408 52.030 -2.068 1.00 41.28      C1
ATOM 2895 CG GLU 434      57.126 53.356 -2.019 1.00 43.07      C1
ATOM 2896 CD GLU 434      57.832 53.516 -0.698 1.00 45.70      C1
ATOM 2897 OE1 GLU 434     57.190 53.538  0.367 1.00 49.33      C1
ATOM 2898 OE2 GLU 434     59.051 53.579 -0.760 1.00 45.45      C1
ATOM 2899 C  GLU 434      58.257 50.348 -1.548 1.00 34.00      C1
ATOM 2900 O  GLU 434      59.388 50.481 -1.983 1.00 32.93      C1
ATOM 2901 N  LYS 435      58.067 49.860 -0.330 1.00 34.34      C1
ATOM 2902 H  LYS 435      57.146 49.837  0.014 1.00  0.00      C1
ATOM 2903 CA LYS 435      59.151 49.358  0.511 1.00 34.56      C1
ATOM 2904 CB LYS 435      58.577 49.010  1.847 1.00 33.89      C1
ATOM 2905 CG LYS 435      58.357 50.231  2.709 1.00 36.71      C1
ATOM 2906 CD LYS 435      58.244 49.748  4.137 1.00 40.31      C1
ATOM 2907 CE LYS 435      58.293 50.861  5.213 1.00 45.32      C1
ATOM 2908 NZ LYS 435      58.494 50.325  6.575 1.00 47.31      C1
ATOM 2909 HZ1 LYS 435     59.388 49.795  6.611 1.00  0.00      C1
ATOM 2910 HZ2 LYS 435     57.708 49.689  6.818 1.00  0.00      C1
ATOM 2911 HZ3 LYS 435     58.534 51.109  7.257 1.00  0.00      C1
ATOM 2912 C  LYS 435      59.906 48.135 -0.065 1.00 36.10      C1
ATOM 2913 O  LYS 435      61.139 48.036 -0.012 1.00 37.08      C1
ATOM 2914 N  LEU 436      59.215 47.168 -0.665 1.00 36.28      C1
ATOM 2915 H  LEU 436      58.235 47.245 -0.651 1.00  0.00      C1
ATOM 2916 CA LEU 436      59.793 45.994 -1.304 1.00 34.25      C1
ATOM 2917 CB LEU 436      58.655 45.076 -1.753 1.00 33.41      C1
ATOM 2918 CG LEU 436      57.920 44.327 -0.610 1.00 34.72      C1
ATOM 2919 CD1 LEU 436     56.764 43.538 -1.181 1.00 33.50      C1
ATOM 2920 CD2 LEU 436     58.880 43.375  0.117 1.00 36.39      C1
ATOM 2921 C  LEU 436      60.669 46.383 -2.467 1.00 33.31      C1
ATOM 2922 O  LEU 436      61.756 45.825 -2.647 1.00 33.94      C1
ATOM 2923 N  CYS 437      60.220 47.374 -3.222 1.00 32.34      C1
ATOM 2924 H  CYS 437      59.290 47.661 -3.097 1.00  0.00      C1
ATOM 2925 CA CYS 437      60.978 47.949 -4.301 1.00 32.01      C1
ATOM 2926 C  CYS 437      62.214 48.704 -3.857 1.00 34.70      C1
ATOM 2927 O  CYS 437      63.313 48.599 -4.412 1.00 36.26      C1
ATOM 2928 CB CYS 437      60.094 48.840 -5.008 1.00 30.97      C1
ATOM 2929 SG CYS 437      61.003 49.666 -6.319 1.00 36.22      C1
ATOM 2930 N  ALA 438      62.016 49.463 -2.785 1.00 36.35      C1
ATOM 2931 H  ALA 438      61.108 49.547 -2.431 1.00  0.00      C1
ATOM 2932 CA ALA 438      63.060 50.226 -2.170 1.00 35.83      C1
ATOM 2933 CB ALA 438      62.440 51.107 -1.153 1.00 36.38      C1
ATOM 2934 C  ALA 438      64.065 49.294 -1.527 1.00 37.01      C1
ATOM 2935 O  ALA 438      65.132 49.168 -2.092 1.00 39.39      C1
ATOM 2936 N  THR 439      63.808 48.591 -0.422 1.00 36.59      C1
ATOM 2937 H  THR 439      62.947 48.723  0.014 1.00  0.00      C1
ATOM 2938 CA THR 439      64.742 47.669  0.223 1.00 35.70      C1
ATOM 2939 CB THR 439      64.073 47.042  1.400 1.00 35.34      C1
ATOM 2940 OG1 THR 439     63.323 48.048  2.040 1.00 38.31      C1
ATOM 2941 HG1 THR 439     62.419 47.999  1.706 1.00  0.00      C1
ATOM 2942 CG2 THR 439     65.039 46.479  2.369 1.00 36.50      C1
ATOM 2943 C  THR 439      65.331 46.517 -0.590 1.00 36.10      C1
ATOM 2944 O  THR 439      66.448 46.093 -0.312 1.00 36.51      C1
ATOM 2945 N  TYR 440      64.603 45.917 -1.548 1.00 36.02      C1
ATOM 2946 H  TYR 440      63.751 46.319 -1.822 1.00  0.00      C1
ATOM 2947 CA TYR 440      65.057 44.691 -2.198 1.00 34.28      C1
ATOM 2948 CB TYR 440      64.175 43.480 -1.878 1.00 33.99      C1
ATOM 2949 CG TYR 440      64.016 43.240 -0.397 1.00 34.14      C1
ATOM 2950 CD1 TYR 440     62.773 43.230  0.169 1.00 35.16      C1
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FIG.5PP

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ATOM 2951 CE1 TYR 440 62.625 43.037 1.532 1.00 36.66 C1
ATOM 2952 CD2 TYR 440 65.126 43.064 0.385 1.00 37.83 C1
ATOM 2953 CE2 TYR 440 64.992 42.881 1.752 1.00 39.02 C1
ATOM 2954 CZ TYR 440 63.741 42.864 2.317 1.00 37.34 C1
ATOM 2955 OH TYR 440 63.637 42.649 3.678 1.00 37.56 C1
ATOM 2956 HH TYR 440 64.498 42.343 3.988 1.00 0.00 C1
ATOM 2957 C TYR 440 65.088 44.768 -3.681 1.00 34.07 C1
ATOM 2958 O TYR 440 65.598 43.823 -4.267 1.00 35.54 C1
ATOM 2959 N LYS 441 64.627 45.833 -4.330 1.00 33.18 C1
ATOM 2960 H LYS 441 64.345 46.623 -3.822 1.00 0.00 C1
ATOM 2961 CA LYS 441 64.595 45.957 -5.763 1.00 30.44 C1
ATOM 2962 CB LYS 441 65.983 45.759 -6.364 1.00 33.76 C1
ATOM 2963 CG LYS 441 66.729 47.080 -6.407 1.00 39.59 C1
ATOM 2964 CD LYS 441 67.273 47.497 -5.045 1.00 47.69 C1
ATOM 2965 CE LYS 441 67.503 49.028 -4.984 1.00 53.37 C1
ATOM 2966 NZ LYS 441 66.267 49.780 -5.240 1.00 57.64 C1
ATOM 2967 HZ1 LYS 441 65.568 49.549 -4.506 1.00 0.00 C1
ATOM 2968 HZ2 LYS 441 65.885 49.525 -6.173 1.00 0.00 C1
ATOM 2969 HZ3 LYS 441 66.468 50.801 -5.219 1.00 0.00 C1
ATOM 2970 C LYS 441 63.629 45.015 -6.425 1.00 28.86 C1
ATOM 2971 O LYS 441 63.791 44.688 -7.603 1.00 29.95 C1
ATOM 2972 N LEU 442 62.556 44.601 -5.749 1.00 27.58 C1
ATOM 2973 H LEU 442 62.392 44.924 -4.837 1.00 0.00 C1
ATOM 2974 CA LEU 442 61.554 43.780 -6.402 1.00 28.82 C1
ATOM 2975 CB LEU 442 60.947 42.694 -5.466 1.00 26.98 C1
ATOM 2976 CG LEU 442 61.905 41.634 -4.847 1.00 27.75 C1
ATOM 2977 CD1 LEU 442 61.133 40.643 -4.009 1.00 24.29 C1
ATOM 2978 CD2 LEU 442 62.667 40.932 -5.963 1.00 19.72 C1
ATOM 2979 C LEU 442 60.575 44.892 -6.635 1.00 30.59 C1
ATOM 2980 O LEU 442 59.811 45.261 -5.741 1.00 32.36 C1
ATOM 2981 N CYS 443 60.700 45.506 -7.804 1.00 32.15 C1
ATOM 2982 H CYS 443 61.423 45.199 -8.389 1.00 0.00 C1
ATOM 2983 CA CYS 443 59.866 46.645 -8.191 1.00 32.69 C1
ATOM 2984 C CYS 443 58.807 46.380 -9.217 1.00 33.43 C1
ATOM 2985 O CYS 443 58.051 47.288 -9.465 1.00 34.10 C1
ATOM 2986 CB CYS 443 60.715 47.800 -8.743 1.00 30.74 C1
ATOM 2987 SG CYS 443 61.938 48.345 -7.519 1.00 32.96 C1
ATOM 2988 N HIS 444 58.649 45.260 -9.911 1.00 35.65 C1
ATOM 2989 H HIS 444 59.147 44.445 -9.659 1.00 0.00 C1
ATOM 2990 CA HIS 444 57.662 45.172 -10.975 1.00 37.75 C1
ATOM 2991 CB HIS 444 58.329 45.224 -12.330 1.00 37.09 C1
ATOM 2992 CG HIS 444 59.149 46.476 -12.560 1.00 41.36 C1
ATOM 2993 CD2 HIS 444 60.434 46.664 -12.075 1.00 41.40 C1
ATOM 2994 ND1 HIS 444 58.811 47.563 -13.261 1.00 41.74 C1
ATOM 2995 HD1 HIS 444 57.892 47.890 -13.410 1.00 0.00 C1
ATOM 2996 CE1 HIS 444 59.850 48.372 -13.217 1.00 42.00 C1
ATOM 2997 NE2 HIS 444 60.817 47.832 -12.502 1.00 41.38 C1
ATOM 2998 HE2 HIS 444 61.690 48.248 -12.334 1.00 0.00 C1
ATOM 2999 C HIS 444 56.889 43.871 -10.878 1.00 40.10 C1
ATOM 3000 O HIS 444 57.461 42.867 -11.309 1.00 40.15 C1
ATOM 3001 N PRO 445 55.615 43.752 -10.406 1.00 42.06 C1
ATOM 3002 CD PRO 445 54.738 44.836 -9.937 1.00 41.56 C1
ATOM 3003 CA PRO 445 54.913 42.497 -10.276 1.00 40.90 C1
ATOM 3004 CB PRO 445 53.569 42.882 -9.730 1.00 39.35 C1
ATOM 3005 CG PRO 445 53.364 44.274 -10.215 1.00 39.35 C1
ATOM 3006 C PRO 445 54.868 41.782 -11.600 1.00 42.18 C1
ATOM 3007 O PRO 445 54.769 40.571 -11.569 1.00 45.69 C1
ATOM 3008 N GLU 446 55.082 42.380 -12.769 1.00 41.64 C1
ATOM 3009 H GLU 446 55.320 43.320 -12.761 1.00 0.00 C1
ATOM 3010 CA GLU 446 55.025 41.656 -14.029 1.00 42.05 C1
ATOM 3011 CB GLU 446 54.967 42.639 -15.183 1.00 47.06 C1
ATOM 3012 CG GLU 446 54.109 43.925 -14.992 1.00 56.71 C1
ATOM 3013 CD GLU 446 54.728 45.083 -14.162 1.00 62.28 C1
ATOM 3014 OE1 GLU 446 54.100 45.472 -13.178 1.00 66.26 C1
ATOM 3015 OE2 GLU 446 55.818 45.604 -14.473 1.00 65.55 C1
ATOM 3016 C GLU 446 56.237 40.722 -14.197 1.00 40.44 C1
ATOM 3017 O GLU 446 56.186 39.708 -14.904 1.00 41.66 C1
ATOM 3018 N GLU 447 57.360 40.995 -13.538 1.00 37.89 C1
ATOM 3019 H GLU 447 57.394 41.809 -12.999 1.00 0.00 C1
ATOM 3020 CA GLU 447 58.519 40.096 -13.509 1.00 36.73 C1
ATOM 3021 CB GLU 447 59.750 40.810 -12.976 1.00 34.60 C1
ATOM 3022 CG GLU 447 60.320 41.883 -13.850 1.00 35.27 C1
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FIG.5QQ

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ATOM 3023 CD GLU 447 61.450 42.699 -13.197 1.00 36.14 C1
ATOM 3024 OE1 GLU 447 62.240 43.286 -13.939 1.00 37.31 C1
ATOM 3025 OE2 GLU 447 61.541 42.782 -11.970 1.00 32.80 C1
ATOM 3026 C GLU 447 58.311 38.850 -12.599 1.00 36.31 C1
ATOM 3027 O GLU 447 59.113 37.911 -12.592 1.00 36.33 C1
ATOM 3028 N LEU 448 57.273 38.763 -11.769 1.00 33.81 C1
ATOM 3029 H LEU 448 56.554 39.431 -11.802 1.00 0.00 C1
ATOM 3030 CA LEU 448 57.145 37.691 -10.839 1.00 31.88 C1
ATOM 3031 CB LEU 448 57.080 38.299 -9.484 1.00 29.29 C1
ATOM 3032 CG LEU 448 58.008 39.432 -9.140 1.00 29.81 C1
ATOM 3033 CD1 LEU 448 57.907 39.863 -7.684 1.00 26.02 C1
ATOM 3034 CD2 LEU 448 59.396 38.931 -9.392 1.00 31.13 C1
ATOM 3035 C LEU 448 55.863 36.977 -11.165 1.00 33.75 C1
ATOM 3036 O LEU 448 55.436 36.145 -10.382 1.00 33.96 C1
ATOM 3037 N VAL 449 55.166 37.233 -12.263 1.00 36.99 C1
ATOM 3038 H VAL 449 55.580 37.800 -12.942 1.00 0.00 C1
ATOM 3039 CA VAL 449 53.819 36.701 -12.472 1.00 41.46 C1
ATOM 3040 CB VAL 449 53.157 37.546 -13.625 1.00 41.56 C1
ATOM 3041 CG1 VAL 449 54.002 37.614 -14.880 1.00 42.22 C1
ATOM 3042 CG2 VAL 449 51.921 36.858 -14.112 1.00 42.01 C1
ATOM 3043 C VAL 449 53.760 35.192 -12.733 1.00 44.81 C1
ATOM 3044 O VAL 449 52.866 34.469 -12.227 1.00 44.54 C1
ATOM 3045 N LEU 450 54.716 34.669 -13.515 1.00 47.21 C1
ATOM 3046 H LEU 450 55.416 35.260 -13.870 1.00 0.00 C1
ATOM 3047 CA LEU 450 54.771 33.243 -13.781 1.00 50.57 C1
ATOM 3048 CB LEU 450 55.942 32.894 -14.628 1.00 50.75 C1
ATOM 3049 CG LEU 450 56.148 33.488 -15.994 1.00 52.39 C1
ATOM 3050 CD1 LEU 450 57.152 32.586 -16.673 1.00 53.05 C1
ATOM 3051 CD2 LEU 450 54.882 33.534 -16.833 1.00 54.10 C1
ATOM 3052 C LEU 450 54.911 32.468 -12.471 1.00 53.83 C1
ATOM 3053 O LEU 450 54.297 31.406 -12.266 1.00 55.62 C1
ATOM 3054 N LEU 451 55.685 33.097 -11.575 1.00 55.46 C1
ATOM 3055 H LEU 451 56.073 33.954 -11.849 1.00 0.00 C1
ATOM 3056 CA LEU 451 55.998 32.654 -10.223 1.00 56.01 C1
ATOM 3057 CB LEU 451 57.137 33.542 -9.731 1.00 55.80 C1
ATOM 3058 CG LEU 451 57.745 33.278 -8.394 1.00 56.96 C1
ATOM 3059 CD1 LEU 451 58.833 32.284 -8.653 1.00 59.12 C1
ATOM 3060 CD2 LEU 451 58.369 34.511 -7.751 1.00 58.27 C1
ATOM 3061 C LEU 451 54.785 32.700 -9.280 1.00 55.96 C1
ATOM 3062 O LEU 451 54.717 31.935 -8.319 1.00 53.74 C1
ATOM 3063 N GLY 452 53.774 33.533 -9.522 1.00 57.52 C1
ATOM 3064 H GLY 452 53.889 34.241 -10.191 1.00 0.00 C1
ATOM 3065 CA GLY 452 52.567 33.515 -8.710 1.00 60.66 C1
ATOM 3066 C GLY 452 51.942 32.137 -8.772 1.00 63.64 C1
ATOM 3067 O GLY 452 51.476 31.593 -7.782 1.00 62.60 C1
ATOM 3068 N HIS 453 52.089 31.545 -9.969 1.00 68.46 C1
ATOM 3069 H HIS 453 52.628 32.040 -10.618 1.00 0.00 C1
ATOM 3070 CA HIS 453 51.606 30.205 -10.326 1.00 72.27 C1
ATOM 3071 CB HIS 453 51.785 29.908 -11.828 1.00 73.84 C1
ATOM 3072 CG HIS 453 51.421 31.061 -12.777 1.00 77.81 C1
ATOM 3073 CD2 HIS 453 50.599 32.148 -12.498 1.00 79.29 C1
ATOM 3074 ND1 HIS 453 51.886 31.244 -14.012 1.00 79.84 C1
ATOM 3075 HD1 HIS 453 52.617 30.739 -14.425 1.00 0.00 C1
ATOM 3076 CE1 HIS 453 51.385 32.382 -14.470 1.00 81.11 C1
ATOM 3077 NE2 HIS 453 50.613 32.923 -13.551 1.00 79.85 C1
ATOM 3078 HE2 HIS 453 50.230 33.825 -13.586 1.00 0.00 C1
ATOM 3079 C HIS 453 52.454 29.235 -9.515 1.00 73.43 C1
ATOM 3080 O HIS 453 51.875 28.531 -8.692 1.00 73.56 C1
ATOM 3081 N SER 454 53.785 29.207 -9.651 1.00 74.64 C1
ATOM 3082 H SER 454 54.214 29.739 -10.351 1.00 0.00 C1
ATOM 3083 CA SER 454 54.639 28.411 -8.765 1.00 77.07 C1
ATOM 3084 CB SER 454 56.123 28.762 -8.980 1.00 77.34 C1
ATOM 3085 OG SER 454 57.095 27.715 -9.124 1.00 75.28 C1
ATOM 3086 HG SER 454 57.149 27.211 -8.306 1.00 0.00 C1
ATOM 3087 C SER 454 54.332 28.608 -7.262 1.00 78.84 C1
ATOM 3088 O SER 454 54.270 27.617 -6.535 1.00 80.57 C1
ATOM 3089 N LEU 455 54.070 29.789 -6.693 1.00 79.72 C1
ATOM 3090 H LEU 455 53.956 30.582 -7.250 1.00 0.00 C1
ATOM 3091 CA LEU 455 53.849 29.915 -5.257 1.00 80.43 C1
ATOM 3092 CB LEU 455 54.085 31.347 -4.838 1.00 80.20 C1
ATOM 3093 CG LEU 455 55.389 31.981 -5.269 1.00 81.67 C1
ATOM 3094 CD1 LEU 455 55.254 33.494 -5.419 1.00 81.36 C1
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FIG.5RR

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ATOM  3095 CD2 LEU  455      56.431  31.579  -4.264  1.00 82.26      C1
ATOM  3096 C   LEU  455      52.438  29.510  -4.848  1.00 81.56      C1
ATOM  3097 O   LEU  455      52.038  29.893  -3.741  1.00 82.22      C1
ATOM  3098 N   GLY  456      51.653  28.816  -5.708  1.00 81.89      C1
ATOM  3099 H   GLY  456      52.026  28.592  -6.584  1.00  0.00      C1
ATOM  3100 CA  GLY  456      50.269  28.361  -5.467  1.00 82.22      C1
ATOM  3101 C   GLY  456      49.220  29.386  -4.973  1.00 82.56      C1
ATOM  3102 O   GLY  456      48.268  28.989  -4.276  1.00 82.38      C1
ATOM  3103 N   ILE  457      49.342  30.697  -5.286  1.00 82.54      C1
ATOM  3104 H   ILE  457      50.075  30.942  -5.894  1.00  0.00      C1
ATOM  3105 CA  ILE  457      48.435  31.761  -4.824  1.00 81.63      C1
ATOM  3106 CB  ILE  457      49.110  33.157  -5.086  1.00 80.69      C1
ATOM  3107 CG2 ILE  457      48.218  34.305  -4.662  1.00 79.76      C1
ATOM  3108 CG1 ILE  457      50.369  33.275  -4.253  1.00 79.82      C1
ATOM  3109 CD  ILE  457      51.506  33.868  -5.081  1.00 77.89      C1
ATOM  3110 C   ILE  457      47.048  31.698  -5.472  1.00 81.70      C1
ATOM  3111 O   ILE  457      46.903  31.761  -6.700  1.00 82.57      C1
ATOM  3112 N   PRO  458      45.963  31.583  -4.705  1.00 81.40      C1
ATOM  3113 CD  PRO  458      45.959  31.225  -3.278  1.00 81.21      C1
ATOM  3114 CA  PRO  458      44.607  31.643  -5.264  1.00 80.74      C1
ATOM  3115 CB  PRO  458      43.779  30.942  -4.157  1.00 81.12      C1
ATOM  3116 CG  PRO  458      44.757  30.293  -3.173  1.00 80.47      C1
ATOM  3117 C   PRO  458      44.120  33.063  -5.648  1.00 79.70      C1
ATOM  3118 O   PRO  458      43.674  33.736  -4.718  1.00 80.10      C1
ATOM  3119 N   TRP  459      44.171  33.662  -6.861  1.00 78.19      C1
ATOM  3120 H   TRP  459      44.614  33.185  -7.591  1.00  0.00      C1
ATOM  3121 CA  TRP  459      43.543  34.986  -7.092  1.00 77.73      C1
ATOM  3122 CB  TRP  459      43.802  35.428  -8.522  1.00 78.71      C1
ATOM  3123 CG  TRP  459      43.054  36.677  -9.017  1.00 81.37      C1
ATOM  3124 CD2 TRP  459      41.802  36.771  -9.618  1.00 82.89      C1
ATOM  3125 CE2 TRP  459      41.717  38.139  -9.883  1.00 84.21      C1
ATOM  3126 CE3 TRP  459      40.738  35.960  -9.983  1.00 84.28      C1
ATOM  3127 CD1 TRP  459      43.661  37.899  -8.925  1.00 83.89      C1
ATOM  3128 NE1 TRP  459      42.828  38.765  -9.460  1.00 85.23      C1
ATOM  3129 HE1 TRP  459      42.944  39.738  -9.483  1.00  0.00      C1
ATOM  3130 CZ2 TRP  459      40.615  38.727 -10.494  1.00 84.17      C1
ATOM  3131 CZ3 TRP  459      39.630  36.538 -10.597  1.00 84.56      C1
ATOM  3132 CH2 TRP  459      39.562  37.904 -10.852  1.00 84.83      C1
ATOM  3133 C   TRP  459      42.009  35.013  -6.827  1.00 77.31      C1
ATOM  3134 O   TRP  459      41.202  34.244  -7.376  1.00 76.38      C1
ATOM  3135 N   ALA  460      41.557  35.969  -6.020  1.00 76.81      C1
ATOM  3136 H   ALA  460      42.187  36.640  -5.689  1.00  0.00      C1
ATOM  3137 CA  ALA  460      40.158  36.044  -5.613  1.00 76.44      C1
ATOM  3138 CB  ALA  460      40.072  36.724  -4.243  1.00 75.51      C1
ATOM  3139 C   ALA  460      39.237  36.784  -6.588  1.00 76.29      C1
ATOM  3140 O   ALA  460      39.449  37.976  -6.833  1.00 76.98      C1
ATOM  3141 N   PRO  461      38.217  36.147  -7.187  1.00 76.26      C1
ATOM  3142 CD  PRO  461      38.104  34.684  -7.245  1.00 75.88      C1
ATOM  3143 CA  PRO  461      37.242  36.793  -8.068  1.00 75.46      C1
ATOM  3144 CB  PRO  461      36.605  35.605  -8.755  1.00 75.71      C1
ATOM  3145 CG  PRO  461      36.703  34.458  -7.767  1.00 75.60      C1
ATOM  3146 C   PRO  461      36.221  37.803  -7.545  1.00 75.72      C1
ATOM  3147 O   PRO  461      35.677  37.734  -6.440  1.00 73.66      C1
ATOM  3148 N   LEU  462      35.996  38.767  -8.449  1.00 77.19      C1
ATOM  3149 H   LEU  462      36.516  38.723  -9.277  1.00  0.00      C1
ATOM  3150 CA  LEU  462      35.069  39.891  -8.275  1.00 78.87      C1
ATOM  3151 CB  LEU  462      35.674  40.984  -7.360  1.00 78.32      C1
ATOM  3152 CG  LEU  462      34.786  41.959  -6.558  1.00 78.09      C1
ATOM  3153 CD1 LEU  462      34.051  42.987  -7.406  1.00 78.32      C1
ATOM  3154 CD2 LEU  462      33.767  41.092  -5.828  1.00 78.62      C1
ATOM  3155 C   LEU  462      34.701  40.565  -9.611  1.00 80.63      C1
ATOM  3156 OT1 LEU  462      33.507  40.842  -9.808  1.00 81.74      C1
ATOM  3157 OT2 LEU  462      35.606  40.847 -10.417  1.00 81.39      C1
ATOM  3158 CB  LEU  472      22.074  42.654  -1.426  1.00 62.24      C2
ATOM  3159 CG  LEU  472      22.278  44.145  -1.189  1.00 59.98      C2
ATOM  3160 CD1 LEU  472      23.496  44.325  -0.328  1.00 59.13      C2
ATOM  3161 CD2 LEU  472      22.501  44.883  -2.486  1.00 56.85      C2
ATOM  3162 C   LEU  472      23.504  40.625  -1.996  1.00 63.91      C2
ATOM  3163 O   LEU  472      23.738  39.874  -2.949  1.00 64.90      C2
ATOM  3164 HT1 LEU  472      21.563  41.441  -3.595  1.00  0.00      C2
ATOM  3165 HT2 LEU  472      23.091  41.291  -4.237  1.00  0.00      C2
ATOM  3166 N   LEU  472      22.472  41.930  -3.693  1.00 64.29      C2
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FIG.5SS

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ATOM  3167 HT3 LEU  472      22.358  42.849  -4.160  1.00  0.00      C2
ATOM  3168 CA  LEU  472      23.092  42.037  -2.386  1.00 63.85      C2
ATOM  3169 N   ALA  473      23.652  40.229  -0.733  1.00 63.02      C2
ATOM  3170 H   ALA  473      23.533  40.867   0.002  1.00  0.00      C2
ATOM  3171 CA  ALA  473      24.023  38.881  -0.353  1.00 62.37      C2
ATOM  3172 CB  ALA  473      22.870  37.939  -0.558  1.00 63.65      C2
ATOM  3173 C   ALA  473      25.196  38.354  -1.126  1.00 62.01      C2
ATOM  3174 O   ALA  473      26.301  38.651  -0.715  1.00 63.36      C2
ATOM  3175 N   GLY  474      25.032  37.784  -2.306  1.00 61.43      C2
ATOM  3176 H   GLY  474      24.148  37.818  -2.722  1.00  0.00      C2
ATOM  3177 CA  GLY  474      26.101  37.137  -3.047  1.00 63.80      C2
ATOM  3178 C   GLY  474      27.354  37.950  -3.356  1.00 65.13      C2
ATOM  3179 O   GLY  474      28.482  37.417  -3.257  1.00 66.24      C2
ATOM  3180 N   CYS  475      27.175  39.237  -3.757  1.00 64.88      C2
ATOM  3181 H   CYS  475      26.261  39.550  -3.885  1.00  0.00      C2
ATOM  3182 CA  CYS  475      28.308  40.127  -4.068  1.00 61.84      C2
ATOM  3183 CB  CYS  475      27.925  41.413  -4.806  1.00 63.74      C2
ATOM  3184 SG  CYS  475      29.494  42.075  -5.437  1.00 68.86      C2
ATOM  3185 C   CYS  475      28.995  40.567  -2.795  1.00 57.30      C2
ATOM  3186 O   CYS  475      30.214  40.449  -2.724  1.00 57.14      C2
ATOM  3187 N   LEU  476      28.230  40.983  -1.779  1.00 53.29      C2
ATOM  3188 H   LEU  476      27.264  41.024  -1.885  1.00  0.00      C2
ATOM  3189 CA  LEU  476      28.797  41.315  -0.493  1.00 50.43      C2
ATOM  3190 CB  LEU  476      27.719  41.723   0.523  1.00 45.68      C2
ATOM  3191 CG  LEU  476      27.130  43.165   0.497  1.00 42.80      C2
ATOM  3192 CD1 LEU  476      26.670  43.559   1.896  1.00 36.25      C2
ATOM  3193 CD2 LEU  476      28.180  44.180   0.057  1.00 40.22      C2
ATOM  3194 C   LEU  476      29.546  40.108   0.042  1.00 50.42      C2
ATOM  3195 O   LEU  476      30.614  40.222   0.646  1.00 50.61      C2
ATOM  3196 N   SER  477      29.053  38.922  -0.270  1.00 50.62      C2
ATOM  3197 H   SER  477      28.196  38.860  -0.729  1.00  0.00      C2
ATOM  3198 CA  SER  477      29.721  37.712   0.125  1.00 51.41      C2
ATOM  3199 CB  SER  477      28.778  36.524  -0.051  1.00 53.45      C2
ATOM  3200 OG  SER  477      27.732  36.616   0.926  1.00 57.65      C2
ATOM  3201 HG  SER  477      27.280  37.462   0.828  1.00  0.00      C2
ATOM  3202 C   SER  477      30.978  37.525  -0.681  1.00 50.75      C2
ATOM  3203 O   SER  477      31.980  37.143  -0.068  1.00 51.41      C2
ATOM  3204 N   GLN  478      31.037  37.788  -1.984  1.00 50.21      C2
ATOM  3205 H   GLN  478      30.222  38.056  -2.457  1.00  0.00      C2
ATOM  3206 CA  GLN  478      32.307  37.697  -2.715  1.00 51.37      C2
ATOM  3207 CB  GLN  478      32.064  37.929  -4.166  1.00 53.65      C2
ATOM  3208 CG  GLN  478      31.983  36.570  -4.788  1.00 57.32      C2
ATOM  3209 CD  GLN  478      31.354  36.649  -6.160  1.00 60.47      C2
ATOM  3210 OE1 GLN  478      31.999  36.504  -7.205  1.00 62.26      C2
ATOM  3211 NE2 GLN  478      30.045  36.878  -6.167  1.00 62.16      C2
ATOM  3212 HE21 GLN  478      29.569  36.972  -5.317  1.00  0.00      C2
ATOM  3213 HE22 GLN  478      29.641  36.928  -7.054  1.00  0.00      C2
ATOM  3214 C   GLN  478      33.398  38.670  -2.249  1.00 50.66      C2
ATOM  3215 O   GLN  478      34.584  38.314  -2.217  1.00 50.13      C2
ATOM  3216 N   LEU  479      33.045  39.909  -1.859  1.00 48.78      C2
ATOM  3217 H   LEU  479      32.131  40.223  -2.039  1.00  0.00      C2
ATOM  3218 CA  LEU  479      34.015  40.800  -1.235  1.00 45.87      C2
ATOM  3219 CB  LEU  479      33.434  42.141  -0.827  1.00 47.03      C2
ATOM  3220 CG  LEU  479      32.853  43.083  -1.818  1.00 49.40      C2
ATOM  3221 CD1 LEU  479      32.596  44.393  -1.078  1.00 48.15      C2
ATOM  3222 CD2 LEU  479      33.779  43.258  -3.000  1.00 48.59      C2
ATOM  3223 C   LEU  479      34.505  40.146   0.056  1.00 42.13      C2
ATOM  3224 O   LEU  479      35.695  39.955   0.262  1.00 40.90      C2
ATOM  3225 N   HIS  480      33.609  39.766   0.950  1.00 39.56      C2
ATOM  3226 H   HIS  480      32.658  39.935   0.763  1.00  0.00      C2
ATOM  3227 CA  HIS  480      33.979  39.108   2.179  1.00 37.81      C2
ATOM  3228 CB  HIS  480      32.742  38.714   2.922  1.00 34.29      C2
ATOM  3229 CG  HIS  480      33.094  38.241   4.309  1.00 33.82      C2
ATOM  3230 CD2 HIS  480      33.123  36.932   4.709  1.00 33.44      C2
ATOM  3231 ND1 HIS  480      33.450  38.995   5.344  1.00 34.27      C2
ATOM  3232 HD1 HIS  480      33.505  39.976   5.362  1.00  0.00      C2
ATOM  3233 CE1 HIS  480      33.706  38.223   6.365  1.00 33.80      C2
ATOM  3234 NE2 HIS  480      33.504  36.986   5.965  1.00 37.12      C2
ATOM  3235 HE2 HIS  480      33.637  36.202   6.544  1.00  0.00      C2
ATOM  3236 C   HIS  480      34.836  37.860   1.961  1.00 39.08      C2
ATOM  3237 O   HIS  480      35.716  37.631   2.791  1.00 40.93      C2
ATOM  3238 N   SER  481      34.615  37.029   0.935  1.00 39.24      C2
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FIG.5TT

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ATOM 3239 H  SER 481  33.900 37.241  0.305 1.00 0.00  C2
ATOM 3240 CA SER 481  35.391 35.818  0.683 1.00 38.17 C2
ATOM 3241 CB SER 481  34.813 34.943 -0.420 1.00 40.42 C2
ATOM 3242 OG SER 481  33.454 34.597 -0.137 1.00 47.61 C2
ATOM 3243 HG SER 481  32.898 35.385 -0.162 1.00 0.00  C2
ATOM 3244 C  SER 481  36.724 36.272  0.211 1.00 36.12 C2
ATOM 3245 O  SER 481  37.692 35.793  0.765 1.00 36.23 C2
ATOM 3246 N  GLY 482  36.786 37.206 -0.744 1.00 36.21 C2
ATOM 3247 H  GLY 482  35.956 37.498 -1.168 1.00 0.00  C2
ATOM 3248 CA GLY 482  38.028 37.792 -1.266 1.00 36.50 C2
ATOM 3249 C  GLY 482  38.958 38.296 -0.151 1.00 36.14 C2
ATOM 3250 O  GLY 482  40.142 37.936 -0.055 1.00 36.65 C2
ATOM 3251 N  LEU 483  38.381 39.084  0.750 1.00 34.04 C2
ATOM 3252 H  LEU 483  37.445 39.326  0.608 1.00 0.00  C2
ATOM 3253 CA LEU 483  39.073 39.593  1.900 1.00 32.07 C2
ATOM 3254 CB LEU 483  38.134 40.442  2.731 1.00 31.17 C2
ATOM 3255 CG LEU 483  37.535 41.687  2.081 1.00 31.11 C2
ATOM 3256 CD1 LEU 483  36.757 42.411  3.156 1.00 30.82 C2
ATOM 3257 CD2 LEU 483  38.599 42.593  1.480 1.00 29.50 C2
ATOM 3258 C  LEU 483  39.600 38.461  2.745 1.00 32.91 C2
ATOM 3259 O  LEU 483  40.752 38.498  3.199 1.00 31.25 C2
ATOM 3260 N  PHE 484  38.767 37.422  2.925 1.00 34.08 C2
ATOM 3261 H  PHE 484  37.900 37.408  2.471 1.00 0.00  C2
ATOM 3262 CA PHE 484  39.105 36.298  3.788 1.00 34.60 C2
ATOM 3263 CB PHE 484  37.975 35.300  3.925 1.00 37.46 C2
ATOM 3264 CG PHE 484  38.268 34.183  4.897 1.00 40.86 C2
ATOM 3265 CD1 PHE 484  38.219 32.884  4.482 1.00 45.62 C2
ATOM 3266 CD2 PHE 484  38.528 34.445  6.210 1.00 43.62 C2
ATOM 3267 CE1 PHE 484  38.421 31.858  5.395 1.00 47.98 C2
ATOM 3268 CE2 PHE 484  38.731 33.427  7.119 1.00 46.78 C2
ATOM 3269 CZ  PHE 484  38.677 32.119  6.720 1.00 48.06 C2
ATOM 3270 C  PHE 484  40.245 35.602  3.113 1.00 33.92 C2
ATOM 3271 O  PHE 484  41.162 35.289  3.826 1.00 34.25 C2
ATOM 3272 N  LEU 485  40.326 35.413  1.799 1.00 32.75 C2
ATOM 3273 H  LEU 485  39.577 35.717  1.250 1.00 0.00  C2
ATOM 3274 CA LEU 485  41.475 34.778  1.163 1.00 33.74 C2
ATOM 3275 CB LEU 485  41.183 34.629 -0.305 1.00 35.35 C2
ATOM 3276 CG LEU 485  42.101 33.962 -1.275 1.00 37.80 C2
ATOM 3277 CD1 LEU 485  41.181 33.404 -2.345 1.00 41.44 C2
ATOM 3278 CD2 LEU 485  43.125 34.903 -1.899 1.00 40.07 C2
ATOM 3279 C  LEU 485  42.740 35.585  1.376 1.00 33.95 C2
ATOM 3280 O  LEU 485  43.766 35.060  1.850 1.00 33.84 C2
ATOM 3281 N  TYR 486  42.609 36.885  1.034 1.00 33.67 C2
ATOM 3282 H  TYR 486  41.757 37.186  0.659 1.00 0.00  C2
ATOM 3283 CA TYR 486  43.662 37.862  1.242 1.00 31.33 C2
ATOM 3284 CB TYR 486  43.210 39.290  0.714 1.00 35.33 C2
ATOM 3285 CG TYR 486  43.300 39.325 -0.825 1.00 33.37 C2
ATOM 3286 CD1 TYR 486  42.154 39.405 -1.579 1.00 32.79 C2
ATOM 3287 CE1 TYR 486  42.228 39.290 -2.944 1.00 33.73 C2
ATOM 3288 CD2 TYR 486  44.533 39.153 -1.445 1.00 34.59 C2
ATOM 3289 CE2 TYR 486  44.618 39.033 -2.818 1.00 34.63 C2
ATOM 3290 CZ  TYR 486  43.451 39.096 -3.562 1.00 35.58 C2
ATOM 3291 OH  TYR 486  43.484 38.880 -4.942 1.00 38.24 C2
ATOM 3292 HH  TYR 486  42.614 39.086 -5.306 1.00 0.00  C2
ATOM 3293 C  TYR 486  44.068 37.905  2.697 1.00 27.39 C2
ATOM 3294 O  TYR 486  45.258 38.007  2.942 1.00 26.06 C2
ATOM 3295 N  GLN 487  43.270 37.691  3.708 1.00 26.95 C2
ATOM 3296 H  GLN 487  42.315 37.545  3.565 1.00 0.00  C2
ATOM 3297 CA GLN 487  43.835 37.646  5.031 1.00 28.33 C2
ATOM 3298 CB GLN 487  42.690 37.578  6.050 1.00 32.66 C2
ATOM 3299 CG GLN 487  43.092 37.979  7.485 1.00 37.50 C2
ATOM 3300 CD GLN 487  43.966 39.252  7.469 1.00 40.54 C2
ATOM 3301 OE1 GLN 487  43.441 40.346  7.292 1.00 40.45 C2
ATOM 3302 NE2 GLN 487  45.305 39.206  7.549 1.00 38.19 C2
ATOM 3303 HE21 GLN 487  45.755 40.057  7.452 1.00 0.00  C2
ATOM 3304 HE22 GLN 487  45.736 38.340  7.702 1.00 0.00  C2
ATOM 3305 C  GLN 487  44.791 36.455  5.207 1.00 28.53 C2
ATOM 3306 O  GLN 487  45.774 36.542  5.964 1.00 28.72 C2
ATOM 3307 N  GLY 488  44.550 35.363  4.454 1.00 28.32 C2
ATOM 3308 H  GLY 488  43.799 35.400  3.824 1.00 0.00  C2
ATOM 3309 CA GLY 488  45.291 34.120  4.557 1.00 26.04 C2
ATOM 3310 C  GLY 488  46.660 34.264  4.033 1.00 25.75 C2
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FIG.5UU

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ATOM   3311  O   GLY   488      47.660  33.946   4.712  1.00 25.86      C2
ATOM   3312  N   LEU   489      46.655  34.798   2.818  1.00 25.05      C2
ATOM   3313  H   LEU   489      45.798  35.062   2.416  1.00  0.00      C2
ATOM   3314  CA  LEU   489      47.911  34.990   2.099  1.00 25.63      C2
ATOM   3315  CB  LEU   489      47.708  35.570   0.725  1.00 27.66      C2
ATOM   3316  CG  LEU   489      46.761  34.755  -0.189  1.00 30.83      C2
ATOM   3317  CD1 LEU   489      46.373  35.506  -1.471  1.00 30.43      C2
ATOM   3318  CD2 LEU   489      47.472  33.454  -0.502  1.00 32.62      C2
ATOM   3319  C   LEU   489      48.783  35.936   2.853  1.00 25.28      C2
ATOM   3320  O   LEU   489      49.973  35.705   2.914  1.00 27.37      C2
ATOM   3321  N   LEU   490      48.237  36.935   3.534  1.00 25.79      C2
ATOM   3322  H   LEU   490      47.267  37.079   3.515  1.00  0.00      C2
ATOM   3323  CA  LEU   490      49.072  37.868   4.220  1.00 25.96      C2
ATOM   3324  CB  LEU   490      48.274  39.139   4.567  1.00 27.96      C2
ATOM   3325  CG  LEU   490      47.823  40.131   3.474  1.00 27.89      C2
ATOM   3326  CD1 LEU   490      46.772  41.019   4.123  1.00 28.03      C2
ATOM   3327  CD2 LEU   490      48.988  40.942   2.899  1.00 28.15      C2
ATOM   3328  C   LEU   490      49.619  37.243   5.459  1.00 27.33      C2
ATOM   3329  O   LEU   490      50.740  37.528   5.865  1.00 26.73      C2
ATOM   3330  N   GLN   491      48.883  36.370   6.111  1.00 29.88      C2
ATOM   3331  H   GLN   491      47.984  36.127   5.799  1.00  0.00      C2
ATOM   3332  CA  GLN   491      49.430  35.809   7.314  1.00 33.01      C2
ATOM   3333  CB  GLN   491      48.305  35.113   8.027  1.00 38.68      C2
ATOM   3334  CG  GLN   491      47.856  35.963   9.197  1.00 46.07      C2
ATOM   3335  CD  GLN   491      46.348  36.262   9.278  1.00 50.83      C2
ATOM   3336  OE1 GLN   491      45.965  37.436   9.402  1.00 51.92      C2
ATOM   3337  NE2 GLN   491      45.425  35.294   9.278  1.00 51.67      C2
ATOM   3338  HE21 GLN   491      45.723  34.353   9.288  1.00  0.00      C2
ATOM   3339  HE22 GLN   491      44.489  35.560   9.286  1.00  0.00      C2
ATOM   3340  C   GLN   491      50.582  34.867   6.986  1.00 33.58      C2
ATOM   3341  O   GLN   491      51.582  34.828   7.715  1.00 34.65      C2
ATOM   3342  N   ALA   492      50.482  34.191   5.824  1.00 34.15      C2
ATOM   3343  H   ALA   492      49.701  34.382   5.264  1.00  0.00      C2
ATOM   3344  CA  ALA   492      51.416  33.177   5.321  1.00 33.64      C2
ATOM   3345  CB  ALA   492      50.818  32.500   4.081  1.00 31.67      C2
ATOM   3346  C   ALA   492      52.802  33.678   4.959  1.00 34.79      C2
ATOM   3347  O   ALA   492      53.789  32.943   4.879  1.00 36.03      C2
ATOM   3348  N   LEU   493      52.885  34.981   4.728  1.00 35.94      C2
ATOM   3349  H   LEU   493      52.060  35.510   4.721  1.00  0.00      C2
ATOM   3350  CA  LEU   493      54.139  35.634   4.426  1.00 34.86      C2
ATOM   3351  CB  LEU   493      53.898  36.990   3.747  1.00 31.36      C2
ATOM   3352  CG  LEU   493      53.127  37.065   2.443  1.00 28.27      C2
ATOM   3353  CD1 LEU   493      52.715  38.495   2.214  1.00 31.74      C2
ATOM   3354  CD2 LEU   493      53.977  36.608   1.285  1.00 28.79      C2
ATOM   3355  C   LEU   493      54.879  35.843   5.721  1.00 36.15      C2
ATOM   3356  O   LEU   493      55.985  36.374   5.694  1.00 36.70      C2
ATOM   3357  N   GLU   494      54.300  35.497   6.855  1.00 38.35      C2
ATOM   3358  H   GLU   494      53.395  35.130   6.836  1.00  0.00      C2
ATOM   3359  CA  GLU   494      54.910  35.648   8.157  1.00 43.14      C2
ATOM   3360  CB  GLU   494      55.621  34.340   8.545  1.00 46.61      C2
ATOM   3361  CG  GLU   494      54.711  33.471   9.419  1.00 53.71      C2
ATOM   3362  CD  GLU   494      54.195  32.160   8.785  1.00 60.27      C2
ATOM   3363  OE1 GLU   494      53.146  31.653   9.230  1.00 63.52      C2
ATOM   3364  OE2 GLU   494      54.839  31.630   7.862  1.00 62.76      C2
ATOM   3365  C   GLU   494      55.865  36.825   8.343  1.00 44.32      C2
ATOM   3366  O   GLU   494      57.055  36.678   8.610  1.00 46.91      C2
ATOM   3367  N   GLY   495      55.358  38.046   8.114  1.00 44.32      C2
ATOM   3368  H   GLY   495      54.450  38.112   7.753  1.00  0.00      C2
ATOM   3369  CA  GLY   495      56.104  39.272   8.368  1.00 42.36      C2
ATOM   3370  C   GLY   495      57.015  39.695   7.238  1.00 42.33      C2
ATOM   3371  O   GLY   495      57.397  40.866   7.220  1.00 42.42      C2
ATOM   3372  N   ILE   496      57.310  38.802   6.279  1.00 41.04      C2
ATOM   3373  H   ILE   496      56.927  37.906   6.374  1.00  0.00      C2
ATOM   3374  CA  ILE   496      58.259  38.993   5.192  1.00 41.15      C2
ATOM   3375  CB  ILE   496      57.929  40.216   4.253  1.00 38.60      C2
ATOM   3376  CG2 ILE   496      59.077  40.437   3.248  1.00 37.62      C2
ATOM   3377  CG1 ILE   496      56.662  39.964   3.480  1.00 36.39      C2
ATOM   3378  CD  ILE   496      56.314  41.071   2.470  1.00 35.27      C2
ATOM   3379  C   ILE   496      59.672  39.203   5.749  1.00 42.91      C2
ATOM   3380  O   ILE   496      60.541  38.396   5.448  1.00 44.22      C2
ATOM   3381  N   SER   497      59.998  40.228   6.533  1.00 44.31      C2
ATOM   3382  H   SER   497      59.297  40.852   6.827  1.00  0.00      C2
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FIG.5VV

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ATOM  3383 CA  SER  497      61.346  40.501   6.992  1.00 44.86      C2
ATOM  3384 CB  SER  497      62.204  41.254   5.938  1.00 44.13      C2
ATOM  3385 OG  SER  497      62.181  42.673   6.033  1.00 40.74      C2
ATOM  3386 HG  SER  497      62.531  42.964   5.170  1.00  0.00      C2
ATOM  3387 C   SER  497      61.164  41.413   8.185  1.00 45.85      C2
ATOM  3388 O   SER  497      60.132  42.110   8.288  1.00 47.55      C2
ATOM  3389 N   PRO  498      62.164  41.490   9.071  1.00 44.96      C2
ATOM  3390 CD  PRO  498      63.338  40.621   9.126  1.00 42.33      C2
ATOM  3391 CA  PRO  498      62.086  42.327  10.250  1.00 44.88      C2
ATOM  3392 CB  PRO  498      63.431  42.038  10.885  1.00 45.13      C2
ATOM  3393 CG  PRO  498      63.629  40.581  10.603  1.00 42.00      C2
ATOM  3394 C   PRO  498      61.760  43.799   9.983  1.00 45.22      C2
ATOM  3395 O   PRO  498      61.215  44.446  10.869  1.00 45.24      C2
ATOM  3396 N   GLU  499      62.017  44.314   8.777  1.00 46.16      C2
ATOM  3397 H   GLU  499      62.362  43.716   8.081  1.00  0.00      C2
ATOM  3398 CA  GLU  499      61.731  45.699   8.391  1.00 48.06      C2
ATOM  3399 CB  GLU  499      62.498  46.193   7.155  1.00 52.19      C2
ATOM  3400 CG  GLU  499      64.001  46.187   7.100  1.00 57.51      C2
ATOM  3401 CD  GLU  499      64.544  44.777   7.076  1.00 60.61      C2
ATOM  3402 OE1 GLU  499      64.755  44.231   8.162  1.00 62.96      C2
ATOM  3403 OE2 GLU  499      64.739  44.234   5.984  1.00 62.79      C2
ATOM  3404 C   GLU  499      60.269  45.896   7.981  1.00 46.94      C2
ATOM  3405 O   GLU  499      59.600  46.895   8.272  1.00 48.15      C2
ATOM  3406 N   LEU  500      59.806  44.934   7.193  1.00 44.38      C2
ATOM  3407 H   LEU  500      60.351  44.137   7.027  1.00  0.00      C2
ATOM  3408 CA  LEU  500      58.491  44.997   6.651  1.00 41.08      C2
ATOM  3409 CB  LEU  500      58.519  44.197   5.445  1.00 41.37      C2
ATOM  3410 CG  LEU  500      59.303  44.862   4.351  1.00 42.70      C2
ATOM  3411 CD1 LEU  500      59.776  43.828   3.351  1.00 43.98      C2
ATOM  3412 CD2 LEU  500      58.427  45.874   3.671  1.00 45.04      C2
ATOM  3413 C   LEU  500      57.455  44.521   7.628  1.00 40.59      C2
ATOM  3414 O   LEU  500      56.274  44.835   7.463  1.00 40.69      C2
ATOM  3415 N   GLY  501      57.866  43.835   8.685  1.00 39.37      C2
ATOM  3416 H   GLY  501      58.808  43.579   8.730  1.00  0.00      C2
ATOM  3417 CA  GLY  501      56.974  43.386   9.734  1.00 39.59      C2
ATOM  3418 C   GLY  501      55.816  44.324  10.092  1.00 39.66      C2
ATOM  3419 O   GLY  501      54.661  44.034   9.777  1.00 40.66      C2
ATOM  3420 N   PRO  502      55.986  45.462  10.742  1.00 39.90      C2
ATOM  3421 CD  PRO  502      57.227  45.908  11.335  1.00 41.18      C2
ATOM  3422 CA  PRO  502      54.912  46.387  11.045  1.00 38.67      C2
ATOM  3423 CB  PRO  502      55.594  47.494  11.791  1.00 39.23      C2
ATOM  3424 CG  PRO  502      56.989  47.405  11.221  1.00 41.36      C2
ATOM  3425 C   PRO  502      54.158  46.849   9.817  1.00 37.54      C2
ATOM  3426 O   PRO  502      52.966  47.139   9.961  1.00 38.36      C2
ATOM  3427 N   THR  503      54.728  46.887   8.609  1.00 35.13      C2
ATOM  3428 H   THR  503      55.663  46.638   8.449  1.00  0.00      C2
ATOM  3429 CA  THR  503      53.940  47.283   7.462  1.00 35.09      C2
ATOM  3430 CB  THR  503      54.832  47.376   6.245  1.00 34.48      C2
ATOM  3431 OG1 THR  503      56.025  48.018   6.668  1.00 38.23      C2
ATOM  3432 HG1 THR  503      55.857  48.946   6.845  1.00  0.00      C2
ATOM  3433 CG2 THR  503      54.197  48.162   5.126  1.00 35.56      C2
ATOM  3434 C   THR  503      52.836  46.252   7.215  1.00 35.37      C2
ATOM  3435 O   THR  503      51.671  46.552   6.915  1.00 37.11      C2
ATOM  3436 N   LEU  504      53.218  44.996   7.380  1.00 34.02      C2
ATOM  3437 H   LEU  504      54.146  44.799   7.647  1.00  0.00      C2
ATOM  3438 CA  LEU  504      52.301  43.912   7.173  1.00 32.50      C2
ATOM  3439 CB  LEU  504      53.127  42.650   7.002  1.00 34.78      C2
ATOM  3440 CG  LEU  504      53.464  42.256   5.601  1.00 34.07      C2
ATOM  3441 CD1 LEU  504      54.163  40.977   5.667  1.00 37.97      C2
ATOM  3442 CD2 LEU  504      52.254  41.865   4.809  1.00 37.34      C2
ATOM  3443 C   LEU  504      51.324  43.821   8.328  1.00 29.54      C2
ATOM  3444 O   LEU  504      50.141  43.562   8.078  1.00 30.40      C2
ATOM  3445 N   ASP  505      51.736  44.106   9.551  1.00 26.09      C2
ATOM  3446 H   ASP  505      52.689  44.269   9.699  1.00  0.00      C2
ATOM  3447 CA  ASP  505      50.798  44.084  10.643  1.00 27.88      C2
ATOM  3448 CB  ASP  505      51.446  44.345  11.926  1.00 29.86      C2
ATOM  3449 CG  ASP  505      52.500  43.312  12.239  1.00 34.64      C2
ATOM  3450 OD1 ASP  505      52.663  42.298  11.534  1.00 41.04      C2
ATOM  3451 OD2 ASP  505      53.179  43.542  13.224  1.00 37.40      C2
ATOM  3452 C   ASP  505      49.661  45.060  10.568  1.00 28.61      C2
ATOM  3453 O   ASP  505      48.566  44.739  11.039  1.00 30.30      C2
ATOM  3454 N   THR  506      49.894  46.242  10.002  1.00 28.29      C2
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FIG.5WW

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ATOM  3455  H   THR   506      50.823  46.493   9.804  1.00  0.00      C2
ATOM  3456  CA  THR   506      48.860  47.225   9.731  1.00 25.74      C2
ATOM  3457  CB  THR   506      49.497  48.556   9.336  1.00 26.14      C2
ATOM  3458  OG1 THR   506      49.944  49.099  10.588  1.00 31.63      C2
ATOM  3459  HG1 THR   506      49.243  49.072  11.246  1.00  0.00      C2
ATOM  3460  CG2 THR   506      48.594  49.517   8.619  1.00 24.46      C2
ATOM  3461  C   THR   506      48.022  46.735   8.615  1.00 24.00      C2
ATOM  3462  O   THR   506      46.817  46.864   8.719  1.00 25.85      C2
ATOM  3463  N   LEU   507      48.554  46.196   7.525  1.00 23.51      C2
ATOM  3464  H   LEU   507      49.527  46.073   7.453  1.00  0.00      C2
ATOM  3465  CA  LEU   507      47.682  45.770   6.434  1.00 23.85      C2
ATOM  3466  CB  LEU   507      48.574  45.408   5.196  1.00 23.33      C2
ATOM  3467  CG  LEU   507      48.010  44.919   3.858  1.00 20.85      C2
ATOM  3468  CD1 LEU   507      46.771  45.650   3.455  1.00 24.13      C2
ATOM  3469  CD2 LEU   507      49.074  45.055   2.842  1.00 20.13      C2
ATOM  3470  C   LEU   507      46.766  44.640   6.880  1.00 24.09      C2
ATOM  3471  O   LEU   507      45.600  44.764   6.541  1.00 25.80      C2
ATOM  3472  N   GLN   508      47.152  43.618   7.661  1.00 24.01      C2
ATOM  3473  H   GLN   508      48.112  43.555   7.866  1.00  0.00      C2
ATOM  3474  CA  GLN   508      46.228  42.625   8.214  1.00 23.71      C2
ATOM  3475  CB  GLN   508      46.961  41.627   9.036  1.00 23.83      C2
ATOM  3476  CG  GLN   508      47.937  40.899   8.173  1.00 31.64      C2
ATOM  3477  CD  GLN   508      48.842  40.080   9.054  1.00 34.00      C2
ATOM  3478  OE1 GLN   508      50.031  40.346   9.161  1.00 38.32      C2
ATOM  3479  NE2 GLN   508      48.321  39.090   9.748  1.00 36.30      C2
ATOM  3480  HE21 GLN   508      47.373  38.880   9.639  1.00  0.00      C2
ATOM  3481  HE22 GLN   508      48.891  38.636  10.406  1.00  0.00      C2
ATOM  3482  C   GLN   508      45.105  43.123   9.111  1.00 24.24      C2
ATOM  3483  O   GLN   508      43.978  42.650   9.014  1.00 24.06      C2
ATOM  3484  N   LEU   509      45.375  44.019  10.090  1.00 26.07      C2
ATOM  3485  H   LEU   509      46.316  44.262  10.222  1.00  0.00      C2
ATOM  3486  CA  LEU   509      44.378  44.640  10.977  1.00 25.71      C2
ATOM  3487  CB  LEU   509      44.993  45.555  12.031  1.00 25.60      C2
ATOM  3488  CG  LEU   509      45.838  44.757  13.042  1.00 29.00      C2
ATOM  3489  CD1 LEU   509      46.658  45.705  13.886  1.00 28.93      C2
ATOM  3490  CD2 LEU   509      44.950  43.919  13.937  1.00 27.94      C2
ATOM  3491  C   LEU   509      43.465  45.471  10.130  1.00 25.17      C2
ATOM  3492  O   LEU   509      42.274  45.411  10.408  1.00 27.22      C2
ATOM  3493  N   ASP   510      43.899  46.208   9.101  1.00 23.77      C2
ATOM  3494  H   ASP   510      44.865  46.277   8.930  1.00  0.00      C2
ATOM  3495  CA  ASP   510      42.955  46.898   8.240  1.00 22.66      C2
ATOM  3496  CB  ASP   510      43.652  47.829   7.306  1.00 25.21      C2
ATOM  3497  CG  ASP   510      44.316  48.966   8.068  1.00 33.01      C2
ATOM  3498  OD1 ASP   510      45.178  49.621   7.477  1.00 34.28      C2
ATOM  3499  OD2 ASP   510      43.988  49.209   9.250  1.00 34.44      C2
ATOM  3500  C   ASP   510      42.104  45.980   7.398  1.00 23.72      C2
ATOM  3501  O   ASP   510      40.897  46.220   7.387  1.00 24.80      C2
ATOM  3502  N   VAL   511      42.632  44.984   6.659  1.00 22.38      C2
ATOM  3503  H   VAL   511      43.611  44.900   6.620  1.00  0.00      C2
ATOM  3504  CA  VAL   511      41.823  44.010   5.961  1.00 21.89      C2
ATOM  3505  CB  VAL   511      42.752  42.924   5.366  1.00 22.71      C2
ATOM  3506  CG1 VAL   511      41.954  41.756   4.792  1.00 20.43      C2
ATOM  3507  CG2 VAL   511      43.529  43.524   4.210  1.00 16.19      C2
ATOM  3508  C   VAL   511      40.827  43.403   6.960  1.00 21.92      C2
ATOM  3509  O   VAL   511      39.625  43.447   6.719  1.00 23.46      C2
ATOM  3510  N   ALA   512      41.258  43.017   8.163  1.00 20.49      C2
ATOM  3511  H   ALA   512      42.216  43.063   8.361  1.00  0.00      C2
ATOM  3512  CA  ALA   512      40.388  42.357   9.108  1.00 20.83      C2
ATOM  3513  CB  ALA   512      41.103  41.974  10.344  1.00 17.89      C2
ATOM  3514  C   ALA   512      39.250  43.205   9.550  1.00 23.89      C2
ATOM  3515  O   ALA   512      38.201  42.668   9.874  1.00 24.61      C2
ATOM  3516  N   ASP   513      39.417  44.539   9.544  1.00 25.96      C2
ATOM  3517  H   ASP   513      40.300  44.888   9.291  1.00  0.00      C2
ATOM  3518  CA  ASP   513      38.374  45.471   9.947  1.00 25.37      C2
ATOM  3519  CB  ASP   513      38.958  46.787  10.373  1.00 26.88      C2
ATOM  3520  CG  ASP   513      39.682  46.679  11.712  1.00 32.35      C2
ATOM  3521  OD1 ASP   513      40.371  47.644  12.058  1.00 35.06      C2
ATOM  3522  OD2 ASP   513      39.580  45.646  12.390  1.00 34.10      C2
ATOM  3523  C   ASP   513      37.392  45.730   8.846  1.00 24.95      C2
ATOM  3524  O   ASP   513      36.185  45.868   9.090  1.00 26.92      C2
ATOM  3525  N   PHE   514      37.867  45.739   7.634  1.00 22.88      C2
ATOM  3526  H   PHE   514      38.829  45.614   7.475  1.00  0.00      C2
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FIG.5XX

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ATOM  3527 CA  PHE  514     36.974  45.922   6.530  1.00 24.09      C2
ATOM  3528 CB  PHE  514     37.812  46.061   5.266  1.00 18.11      C2
ATOM  3529 CG  PHE  514     36.956  46.470   4.072  1.00 17.86      C2
ATOM  3530 CD1 PHE  514     35.715  47.089   4.245  1.00 15.18      C2
ATOM  3531 CD2 PHE  514     37.440  46.197   2.804  1.00 13.77      C2
ATOM  3532 CE1 PHE  514     34.983  47.419   3.130  1.00 14.53      C2
ATOM  3533 CE2 PHE  514     36.693  46.539   1.705  1.00 12.10      C2
ATOM  3534 CZ  PHE  514     35.468  47.146   1.868  1.00 10.68      C2
ATOM  3535 C   PHE  514     36.026  44.703   6.450  1.00 29.23      C2
ATOM  3536 O   PHE  514     34.788  44.828   6.350  1.00 29.80      C2
ATOM  3537 N   ALA  515     36.604  43.490   6.531  1.00 31.15      C2
ATOM  3538 H   ALA  515     37.581  43.450   6.639  1.00  0.00      C2
ATOM  3539 CA  ALA  515     35.839  42.260   6.416  1.00 32.36      C2
ATOM  3540 CB  ALA  515     36.851  41.126   6.402  1.00 32.35      C2
ATOM  3541 C   ALA  515     34.801  42.089   7.535  1.00 32.39      C2
ATOM  3542 O   ALA  515     33.676  41.609   7.331  1.00 32.63      C2
ATOM  3543 N   THR  516     35.164  42.457   8.735  1.00 33.01      C2
ATOM  3544 H   THR  516     36.117  42.578   8.935  1.00  0.00      C2
ATOM  3545 CA  THR  516     34.231  42.566   9.821  1.00 35.18      C2
ATOM  3546 CB  THR  516     35.016  43.018  10.988  1.00 35.40      C2
ATOM  3547 OG1 THR  516     35.685  41.818  11.336  1.00 42.65      C2
ATOM  3548 HG1 THR  516     36.505  41.713  10.816  1.00  0.00      C2
ATOM  3549 CG2 THR  516     34.262  43.672  12.097  1.00 35.56      C2
ATOM  3550 C   THR  516     33.140  43.554   9.482  1.00 37.62      C2
ATOM  3551 O   THR  516     32.005  43.315   9.857  1.00 40.37      C2
ATOM  3552 N   THR  517     33.387  44.666   8.802  1.00 38.61      C2
ATOM  3553 H   THR  517     34.291  44.850   8.469  1.00  0.00      C2
ATOM  3554 CA  THR  517     32.359  45.641   8.512  1.00 38.92      C2
ATOM  3555 CB  THR  517     33.123  46.903   7.962  1.00 40.46      C2
ATOM  3556 OG1 THR  517     33.832  47.429   9.103  1.00 43.22      C2
ATOM  3557 HG1 THR  517     34.536  46.815   9.335  1.00  0.00      C2
ATOM  3558 CG2 THR  517     32.232  47.926   7.253  1.00 39.90      C2
ATOM  3559 C   THR  517     31.343  45.012   7.551  1.00 38.30      C2
ATOM  3560 O   THR  517     30.137  45.125   7.811  1.00 38.69      C2
ATOM  3561 N   ILE  518     31.790  44.344   6.466  1.00 37.54      C2
ATOM  3562 H   ILE  518     32.756  44.386   6.297  1.00  0.00      C2
ATOM  3563 CA  ILE  518     30.923  43.646   5.510  1.00 36.10      C2
ATOM  3564 CB  ILE  518     31.699  42.912   4.439  1.00 33.81      C2
ATOM  3565 CG2 ILE  518     30.703  42.202   3.555  1.00 33.46      C2
ATOM  3566 CG1 ILE  518     32.623  43.842   3.699  1.00 32.91      C2
ATOM  3567 CD  ILE  518     32.019  44.700   2.596  1.00 34.89      C2
ATOM  3568 C   ILE  518     30.172  42.591   6.317  1.00 38.63      C2
ATOM  3569 O   ILE  518     28.938  42.545   6.205  1.00 39.93      C2
ATOM  3570 N   TRP  519     30.842  41.785   7.179  1.00 38.64      C2
ATOM  3571 H   TRP  519     31.785  41.959   7.361  1.00  0.00      C2
ATOM  3572 CA  TRP  519     30.144  40.784   7.945  1.00 38.15      C2
ATOM  3573 CB  TRP  519     31.124  40.083   8.780  1.00 38.52      C2
ATOM  3574 CG  TRP  519     30.493  38.793   9.255  1.00 42.26      C2
ATOM  3575 CD2 TRP  519     29.880  38.578  10.473  1.00 41.70      C2
ATOM  3576 CE2 TRP  519     29.437  37.278  10.335  1.00 41.69      C2
ATOM  3577 CE3 TRP  519     29.648  39.282  11.629  1.00 42.26      C2
ATOM  3578 CD1 TRP  519     30.448  37.695   8.419  1.00 42.92      C2
ATOM  3579 NE1 TRP  519     29.788  36.793   9.115  1.00 44.19      C2
ATOM  3580 HE1 TRP  519     29.485  35.935   8.741  1.00  0.00      C2
ATOM  3581 CZ2 TRP  519     28.753  36.671  11.360  1.00 41.91      C2
ATOM  3582 CZ3 TRP  519     28.964  38.666  12.652  1.00 41.77      C2
ATOM  3583 CH2 TRP  519     28.522  37.375  12.515  1.00 41.05      C2
ATOM  3584 C   TRP  519     29,027  41.368   8.815  1.00 39.33      C2
ATOM  3585 O   TRP  519     27.888  40.919   8.726  1.00 38.28      C2
ATOM  3586 N   GLN  520     29.264  42.375   9.650  1.00 41.86      C2
ATOM  3587 H   GLN  520     30.180  42.717   9.700  1.00  0.00      C2
ATOM  3588 CA  GLN  520     28.240  43.016  10.464  1.00 44.63      C2
ATOM  3589 CB  GLN  520     28.691  44.198  11.239  1.00 47.03      C2
ATOM  3590 CG  GLN  520     29.602  43.808  12.360  1.00 54.78      C2
ATOM  3591 CD  GLN  520     29.910  45.009  13.243  1.00 60.14      C2
ATOM  3592 OE1 GLN  520     28.988  45.566  13.854  1.00 61.62      C2
ATOM  3593 NE2 GLN  520     31.172  45.456  13.371  1.00 60.46      C2
ATOM  3594 HE21 GLN  520    31.289  46.260  13.910  1.00  0.00      C2
ATOM  3595 HE22 GLN  520    31.895  44.966  12.932  1.00  0.00      C2
ATOM  3596 C   GLN  520     27.141  43.577   9.621  1.00 46.28      C2
ATOM  3597 O   GLN  520     26.001  43.474  10.059  1.00 48.62      C2
ATOM  3598 N   GLN  521     27.362  44.145   8.442  1.00 46.99      C2
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FIG.5YY

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ATOM 3599 H  GLN 521  28.272 44.257  8.092 1.00 0.00  C2
ATOM 3600 CA GLN 521  26.226 44.638  7.716 1.00 49.02 C2
ATOM 3601 CB GLN 521  26.632 45.553  6.566 1.00 50.06 C2
ATOM 3602 CG GLN 521  25.456 46.226  5.790 1.00 50.87 C2
ATOM 3603 CD GLN 521  24.616 47.278  6.534 1.00 51.82 C2
ATOM 3604 OE1 GLN 521  24.864 47.694  7.671 1.00 52.47 C2
ATOM 3605 NE2 GLN 521  23.577 47.776  5.888 1.00 50.36 C2
ATOM 3606 HE21 GLN 521  23.392 47.455  4.987 1.00 0.00 C2
ATOM 3607 HE22 GLN 521  23.044 48.424  6.390 1.00 0.00 C2
ATOM 3608 C  GLN 521  25.454 43.446  7.155 1.00 50.15 C2
ATOM 3609 O  GLN 521  24.214 43.514  7.177 1.00 51.82 C2
ATOM 3610 N  MET 522  26.057 42.348  6.668 1.00 49.18 C2
ATOM 3611 H  MET 522  27.038 42.291  6.688 1.00 0.00  C2
ATOM 3612 CA MET 522  25.280 41.227  6.171 1.00 48.22 C2
ATOM 3613 CB MET 522  26.185 40.167  5.607 1.00 46.36 C2
ATOM 3614 CG MET 522  26.942 40.661  4.412 1.00 44.32 C2
ATOM 3615 SD MET 522  27.855 39.435  3.426 1.00 48.35 C2
ATOM 3616 CE MET 522  28.795 38.447  4.565 1.00 42.80 C2
ATOM 3617 C  MET 522  24.453 40.642  7.316 1.00 50.14 C2
ATOM 3618 O  MET 522  23.380 40.124  7.038 1.00 50.60 C2
ATOM 3619 N  GLU 523  24.848 40.722  8.596 1.00 51.91 C2
ATOM 3620 H  GLU 523  25.766 41.031  8.769 1.00 0.00  C2
ATOM 3621 CA GLU 523  24.027 40.313  9.718 1.00 54.53 C2
ATOM 3622 CB GLU 523  24.654 40.486 11.081 1.00 54.60 C2
ATOM 3623 CG GLU 523  25.732 39.525 11.398 1.00 57.05 C2
ATOM 3624 CD GLU 523  25.386 38.150 10.888 1.00 61.72 C2
ATOM 3625 OE1 GLU 523  24.515 37.487 11.477 1.00 64.60 C2
ATOM 3626 OE2 GLU 523  25.979 37.773  9.872 1.00 63.19 C2
ATOM 3627 C  GLU 523  22.773 41.116  9.836 1.00 58.29 C2
ATOM 3628 O  GLU 523  21.688 40.538  9.850 1.00 59.32 C2
ATOM 3629 N  ALA 524  22.920 42.432  9.992 1.00 61.41 C2
ATOM 3630 H  ALA 524  23.834 42.798 10.024 1.00 0.00  C2
ATOM 3631 CA ALA 524  21.815 43.360 10.076 1.00 63.58 C2
ATOM 3632 CB ALA 524  22.382 44.768  9.992 1.00 64.11 C2
ATOM 3633 C  ALA 524  20.818 43.109  8.946 1.00 64.79 C2
ATOM 3634 O  ALA 524  19.655 42.824  9.206 1.00 65.69 C2
ATOM 3635 N  ALA 525  21.251 43.083  7.693 1.00 66.44 C2
ATOM 3636 H  ALA 525  22.196 43.283  7.516 1.00 0.00  C2
ATOM 3637 CA ALA 525  20.371 42.789  6.574 1.00 68.58 C2
ATOM 3638 CB ALA 525  21.117 43.044  5.288 1.00 67.42 C2
ATOM 3639 C  ALA 525  19.841 41.356  6.558 1.00 71.11 C2
ATOM 3640 O  ALA 525  19.116 40.946  5.651 1.00 71.65 C2
ATOM 3641 N  GLY 526  20.257 40.510  7.498 1.00 74.20 C2
ATOM 3642 H  GLY 526  21.019 40.780  8.043 1.00 0.00  C2
ATOM 3643 CA GLY 526  19.728 39.157  7.653 1.00 76.30 C2
ATOM 3644 C  GLY 526  20.430 38.085  6.842 1.00 78.19 C2
ATOM 3645 O  GLY 526  20.174 36.910  7.094 1.00 79.05 C2
ATOM 3646 N  MET 527  21.388 38.433  5.970 1.00 80.23 C2
ATOM 3647 H  MET 527  21.759 39.337  6.075 1.00 0.00  C2
ATOM 3648 CA MET 527  22.055 37.489  5.063 1.00 81.73 C2
ATOM 3649 CB MET 527  22.771 38.256  3.928 1.00 81.72 C2
ATOM 3650 CG MET 527  22.385 39.719  3.720 1.00 83.52 C2
ATOM 3651 SD MET 527  23.364 40.523  2.436 1.00 87.64 C2
ATOM 3652 CE MET 527  22.600 42.117  2.409 1.00 84.47 C2
ATOM 3653 C  MET 527  23.078 36.584  5.780 1.00 82.64 C2
ATOM 3654 OT1 MET 527  22.974 35.357  5.624 1.00 83.38 C2
ATOM 3655 OT2 MET 527  23.949 37.104  6.500 1.00 82.90 C2
ATOM 3656 CB MET 538  47.224 28.531  2.401 1.00 77.43 C3
ATOM 3657 CG MET 538  47.397 30.041  2.427 1.00 77.15 C3
ATOM 3658 SD MET 538  46.205 30.708  3.604 1.00 79.03 C3
ATOM 3659 CE MET 538  44.850 31.067  2.515 1.00 77.20 C3
ATOM 3660 C  MET 538  48.549 27.839  0.386 1.00 75.32 C3
ATOM 3661 O  MET 538  49.130 26.745  0.405 1.00 77.11 C3
ATOM 3662 HT1 MET 538  47.563 26.068  1.449 1.00 0.00 C3
ATOM 3663 HT2 MET 538  46.638 26.204  0.075 1.00 0.00 C3
ATOM 3664 N  MET 538  46.724 26.552  1.050 1.00 77.52 C3
ATOM 3665 HT3 MET 538  45.873 26.401  1.617 1.00 0.00 C3
ATOM 3666 CA MET 538  47.153 27.940  0.995 1.00 76.57 C3
ATOM 3667 N  PRO 539  49.089 28.870 -0.224 1.00 72.65 C3
ATOM 3668 CD PRO 539  48.346 29.821 -1.046 1.00 72.26 C3
ATOM 3669 CA PRO 539  50.526 29.020 -0.349 1.00 70.34 C3
ATOM 3670 CB PRO 539  50.677 30.365 -1.006 1.00 71.39 C3
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FIG.5ZZ

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ATOM 3671 CG PRO 539 49.437 30.503 -1.837 1.00 71.52 C3
ATOM 3672 C PRO 539 51.250 28.931 0.991 1.00 67.83 C3
ATOM 3673 O PRO 539 50.666 29.294 2.029 1.00 68.05 C3
ATOM 3674 N ALA 540 52.484 28.417 0.961 1.00 64.48 C3
ATOM 3675 H ALA 540 52.858 28.098 0.111 1.00 0.00 C3
ATOM 3676 CA ALA 540 53.389 28.498 2.112 1.00 61.83 C3
ATOM 3677 CB ALA 540 54.004 27.200 2.619 1.00 63.57 C3
ATOM 3678 C ALA 540 54.559 29.212 1.496 1.00 58.74 C3
ATOM 3679 O ALA 540 54.835 29.036 0.301 1.00 58.30 C3
ATOM 3680 N PHE 541 55.256 30.008 2.292 1.00 55.25 C3
ATOM 3681 H PHE 541 55.093 30.068 3.257 1.00 0.00 C3
ATOM 3682 CA PHE 541 56.299 30.814 1.702 1.00 51.38 C3
ATOM 3683 CB PHE 541 55.964 32.306 1.942 1.00 48.80 C3
ATOM 3684 CG PHE 541 54.789 32.703 1.058 1.00 45.77 C3
ATOM 3685 CD1 PHE 541 54.992 32.939 -0.279 1.00 44.20 C3
ATOM 3686 CD2 PHE 541 53.507 32.747 1.582 1.00 44.76 C3
ATOM 3687 CE1 PHE 541 53.901 33.207 -1.074 1.00 43.98 C3
ATOM 3688 CE2 PHE 541 52.428 33.018 0.769 1.00 42.86 C3
ATOM 3689 CZ PHE 541 52.625 33.247 -0.563 1.00 42.52 C3
ATOM 3690 C PHE 541 57.586 30.364 2.333 1.00 49.80 C3
ATOM 3691 O PHE 541 58.002 30.807 3.395 1.00 49.55 C3
ATOM 3692 N ALA 542 58.172 29.442 1.562 1.00 48.21 C3
ATOM 3693 H ALA 542 57.825 29.298 0.656 1.00 0.00 C3
ATOM 3694 CA ALA 542 59.326 28.711 1.968 1.00 45.37 C3
ATOM 3695 CB ALA 542 59.700 27.749 0.898 1.00 45.21 C3
ATOM 3696 C ALA 542 60.510 29.567 2.266 1.00 44.87 C3
ATOM 3697 O ALA 542 61.001 29.504 3.374 1.00 46.49 C3
ATOM 3698 N SER 543 61.013 30.408 1.395 1.00 42.63 C3
ATOM 3699 H SER 543 60.477 30.685 0.630 1.00 0.00 C3
ATOM 3700 CA SER 543 62.253 31.108 1.708 1.00 40.31 C3
ATOM 3701 CB SER 543 63.170 30.861 0.587 1.00 37.74 C3
ATOM 3702 OG SER 543 62.391 31.181 -0.554 1.00 35.74 C3
ATOM 3703 HG SER 543 61.824 30.423 -0.751 1.00 0.00 C3
ATOM 3704 C SER 543 62.087 32.613 1.896 1.00 40.88 C3
ATOM 3705 O SER 543 61.016 33.115 1.536 1.00 42.63 C3
ATOM 3706 N ALA 544 63.120 33.383 2.310 1.00 38.84 C3
ATOM 3707 H ALA 544 63.929 32.951 2.650 1.00 0.00 C3
ATOM 3708 CA ALA 544 63.035 34.836 2.345 1.00 37.31 C3
ATOM 3709 CB ALA 544 64.340 35.450 2.808 1.00 35.74 C3
ATOM 3710 C ALA 544 62.723 35.372 0.947 1.00 37.06 C3
ATOM 3711 O ALA 544 61.829 36.220 0.820 1.00 38.23 C3
ATOM 3712 N PHE 545 63.357 34.881 -0.130 1.00 35.72 C3
ATOM 3713 H PHE 545 64.131 34.298 -0.010 1.00 0.00 C3
ATOM 3714 CA PHE 545 62.992 35.268 -1.484 1.00 33.66 C3
ATOM 3715 CB PHE 545 63.738 34.534 -2.593 1.00 29.71 C3
ATOM 3716 CG PHE 545 63.140 34.742 -3.990 1.00 29.62 C3
ATOM 3717 CD1 PHE 545 62.317 33.788 -4.557 1.00 29.80 C3
ATOM 3718 CD2 PHE 545 63.371 35.915 -4.689 1.00 31.90 C3
ATOM 3719 CE1 PHE 545 61.723 33.984 -5.795 1.00 28.61 C3
ATOM 3720 CE2 PHE 545 62.777 36.113 -5.928 1.00 31.00 C3
ATOM 3721 CZ PHE 545 61.955 35.150 -6.480 1.00 31.01 C3
ATOM 3722 C PHE 545 61.543 34.900 -1.667 1.00 34.81 C3
ATOM 3723 O PHE 545 60.901 35.660 -2.389 1.00 38.88 C3
ATOM 3724 N GLN 546 60.912 33.847 -1.135 1.00 34.77 C3
ATOM 3725 H GLN 546 61.396 33.223 -0.558 1.00 0.00 C3
ATOM 3726 CA GLN 546 59.490 33.637 -1.433 1.00 33.72 C3
ATOM 3727 CB GLN 546 59.145 32.232 -1.140 1.00 34.85 C3
ATOM 3728 CG GLN 546 59.582 31.585 -2.444 1.00 42.45 C3
ATOM 3729 CD GLN 546 59.374 30.085 -2.473 1.00 46.05 C3
ATOM 3730 OE1 GLN 546 59.287 29.472 -1.399 1.00 48.90 C3
ATOM 3731 NE2 GLN 546 59.339 29.442 -3.644 1.00 47.20 C3
ATOM 3732 HE21 GLN 546 59.476 29.948 -4.472 1.00 0.00 C3
ATOM 3733 HE22 GLN 546 59.154 28.481 -3.609 1.00 0.00 C3
ATOM 3734 C GLN 546 58.504 34.541 -0.729 1.00 31.62 C3
ATOM 3735 O GLN 546 57.429 34.850 -1.233 1.00 29.88 C3
ATOM 3736 N ARG 547 58.907 34.929 0.465 1.00 31.09 C3
ATOM 3737 H ARG 547 59.750 34.566 0.811 1.00 0.00 C3
ATOM 3738 CA ARG 547 58.160 35.830 1.282 1.00 31.43 C3
ATOM 3739 CB ARG 547 58.813 35.874 2.601 1.00 31.74 C3
ATOM 3740 CG ARG 547 57.906 35.224 3.623 1.00 37.02 C3
ATOM 3741 CD ARG 547 58.344 33.858 4.076 1.00 40.56 C3
ATOM 3742 NE ARG 547 59.743 34.058 4.345 1.00 47.90 C3
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FIG.5AA

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ATOM  3743 HE  ARG 547     60.389  33.924   3.620  1.00  0.00      C3
ATOM  3744 CZ  ARG 547     60.190  34.394   5.543  1.00 49.48      C3
ATOM  3745 NH1 ARG 547     59.361  34.522   6.593  1.00 51.97      C3
ATOM  3746 HH11 ARG 547    58.380  34.356   6.488  1.00  0.00      C3
ATOM  3747 HH12 ARG 547    59.731  34.763   7.491  1.00  0.00      C3
ATOM  3748 NH2 ARG 547     61.464  34.775   5.616  1.00 48.55      C3
ATOM  3749 HH21 ARG 547    62.025  34.803   4.788  1.00  0.00      C3
ATOM  3750 HH22 ARG 547    61.854  35.034   6.501  1.00  0.00      C3
ATOM  3751 C   ARG 547     58.167  37.181   0.590  1.00 32.26      C3
ATOM  3752 O   ARG 547     57.084  37.694   0.317  1.00 34.25      C3
ATOM  3753 N   ARG 548     59.348  37.717   0.205  1.00 31.44      C3
ATOM  3754 H   ARG 548     60.148  37.203   0.444  1.00  0.00      C3
ATOM  3755 CA  ARG 548     59.529  38.980  -0.555  1.00 30.01      C3
ATOM  3756 CB  ARG 548     60.995  39.213  -0.949  1.00 25.42      C3
ATOM  3757 CG  ARG 548     61.820  39.361   0.294  1.00 26.11      C3
ATOM  3758 CD  ARG 548     63.280  39.158  -0.054  1.00 29.34      C3
ATOM  3759 NE  ARG 548     64.044  39.162   1.189  1.00 32.30      C3
ATOM  3760 HE  ARG 548     63.572  38.883   1.995  1.00  0.00      C3
ATOM  3761 CZ  ARG 548     65.344  39.518   1.325  1.00 32.66      C3
ATOM  3762 NH1 ARG 548     66.159  39.923   0.335  1.00 34.98      C3
ATOM  3763 HH11 ARG 548    67.107  40.170   0.533  1.00  0.00      C3
ATOM  3764 HH12 ARG 548    65.812  39.981  -0.600  1.00  0.00      C3
ATOM  3765 NH2 ARG 548     65.837  39.518   2.549  1.00 32.03      C3
ATOM  3766 HH21 ARG 548    66.788  39.783   2.708  1.00  0.00      C3
ATOM  3767 HH22 ARG 548    65.250  39.275   3.321  1.00  0.00      C3
ATOM  3768 C   ARG 548     58.713  38.997  -1.832  1.00 29.81      C3
ATOM  3769 O   ARG 548     57.778  39.790  -1.968  1.00 33.03      C3
ATOM  3770 N   ALA 549     58.979  38.102  -2.761  1.00 27.87      C3
ATOM  3771 H   ALA 549     59.684  37.436  -2.601  1.00  0.00      C3
ATOM  3772 CA  ALA 549     58.227  38.045  -3.984  1.00 27.18      C3
ATOM  3773 CB  ALA 549     58.797  36.934  -4.857  1.00 28.72      C3
ATOM  3774 C   ALA 549     56.748  37.810  -3.770  1.00 25.91      C3
ATOM  3775 O   ALA 549     55.896  38.337  -4.468  1.00 26.03      C3
ATOM  3776 N   GLY 550     56.421  37.074  -2.748  1.00 26.53      C3
ATOM  3777 H   GLY 550     57.103  36.657  -2.185  1.00  0.00      C3
ATOM  3778 CA  GLY 550     55.055  36.805  -2.457  1.00 26.08      C3
ATOM  3779 C   GLY 550     54.410  38.098  -2.075  1.00 26.94      C3
ATOM  3780 O   GLY 550     53.339  38.380  -2.608  1.00 26.59      C3
ATOM  3781 N   GLY 551     55.073  38.917  -1.234  1.00 27.78      C3
ATOM  3782 H   GLY 551     55.958  38.642  -0.925  1.00  0.00      C3
ATOM  3783 CA  GLY 551     54.540  40.212  -0.779  1.00 26.51      C3
ATOM  3784 C   GLY 551     54.302  41.113  -1.994  1.00 26.82      C3
ATOM  3785 O   GLY 551     53.313  41.852  -2.065  1.00 27.82      C3
ATOM  3786 N   VAL 552     55.154  41.013  -3.012  1.00 25.81      C3
ATOM  3787 H   VAL 552     55.916  40.396  -2.954  1.00  0.00      C3
ATOM  3788 CA  VAL 552     54.952  41.843  -4.176  1.00 28.39      C3
ATOM  3789 CB  VAL 552     56.178  41.743  -5.190  1.00 26.20      C3
ATOM  3790 CG1 VAL 552     55.917  42.391  -6.541  1.00 26.53      C3
ATOM  3791 CG2 VAL 552     57.327  42.546  -4.594  1.00 26.44      C3
ATOM  3792 C   VAL 552     53.650  41.406  -4.820  1.00 29.05      C3
ATOM  3793 O   VAL 552     52.744  42.251  -4.888  1.00 31.68      C3
ATOM  3794 N   LEU 553     53.455  40.120  -5.176  1.00 27.20      C3
ATOM  3795 H   LEU 553     54.122  39.447  -4.908  1.00  0.00      C3
ATOM  3796 CA  LEU 553     52.266  39.705  -5.915  1.00 23.80      C3
ATOM  3797 CB  LEU 553     52.357  38.262  -6.363  1.00 24.86      C3
ATOM  3798 CG  LEU 553     53.432  37.955  -7.357  1.00 23.06      C3
ATOM  3799 CD1 LEU 553     54.073  36.623  -7.092  1.00 24.31      C3
ATOM  3800 CD2 LEU 553     52.794  38.061  -8.703  1.00 21.87      C3
ATOM  3801 C   LEU 553     51.012  39.825  -5.114  1.00 23.72      C3
ATOM  3802 O   LEU 553     49.982  40.138  -5.712  1.00 24.63      C3
ATOM  3803 N   VAL 554     50.962  39.580  -3.803  1.00 24.37      C3
ATOM  3804 H   VAL 554     51.774  39.350  -3.295  1.00  0.00      C3
ATOM  3805 CA  VAL 554     49.660  39.691  -3.180  1.00 26.36      C3
ATOM  3806 CB  VAL 554     49.472  38.751  -1.802  1.00 26.55      C3
ATOM  3807 CG1 VAL 554     50.696  37.933  -1.418  1.00 23.95      C3
ATOM  3808 CG2 VAL 554     48.953  39.614  -0.682  1.00 25.58      C3
ATOM  3809 C   VAL 554     49.322  41.175  -2.960  1.00 27.53      C3
ATOM  3810 O   VAL 554     48.142  41.502  -3.192  1.00 27.44      C3
ATOM  3811 N   ALA 555     50.277  42.106  -2.716  1.00 28.04      C3
ATOM  3812 H   ALA 555     51.221  41.831  -2.658  1.00  0.00      C3
ATOM  3813 CA  ALA 555     49.956  43.539  -2.509  1.00 28.57      C3
ATOM  3814 CB  ALA 555     51.161  44.427  -2.217  1.00 28.07      C3
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FIG.5BBB

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ATOM 3815 C  ALA 555  49.402 44.055 -3.803 1.00 28.12  C3
ATOM 3816 O  ALA 555  48.425 44.803 -3.847 1.00 30.12  C3
ATOM 3817 N  SER 556  49.985 43.521 -4.839 1.00 26.44  C3
ATOM 3818 H  SER 556  50.781 42.956 -4.710 1.00  0.00  C3
ATOM 3819 CA SER 556  49.548 43.810 -6.152 1.00 30.09  C3
ATOM 3820 CB SER 556  50.684 43.277 -6.965 1.00 31.42  C3
ATOM 3821 OG SER 556  50.442 43.338 -8.344 1.00 37.88  C3
ATOM 3822 HG SER 556  49.966 44.144 -8.576 1.00  0.00  C3
ATOM 3823 C  SER 556  48.143 43.243 -6.454 1.00 32.78  C3
ATOM 3824 O  SER 556  47.287 43.961 -7.003 1.00 34.56  C3
ATOM 3825 N  HIS 557  47.750 42.019 -6.088 1.00 32.78  C3
ATOM 3826 H  HIS 557  48.350 41.453 -5.560 1.00  0.00  C3
ATOM 3827 CA HIS 557  46.396 41.605 -6.401 1.00 33.64  C3
ATOM 3828 CB HIS 557  46.203 40.142 -6.242 1.00 37.88  C3
ATOM 3829 CG HIS 557  46.986 39.518 -7.348 1.00 42.44  C3
ATOM 3830 CD2 HIS 557  46.694 39.665 -8.675 1.00 43.63  C3
ATOM 3831 ND1 HIS 557  48.108 38.837 -7.209 1.00 45.23  C3
ATOM 3832 HD1 HIS 557  48.641 38.764 -6.385 1.00  0.00  C3
ATOM 3833 CE1 HIS 557  48.524 38.569 -8.414 1.00 46.56  C3
ATOM 3834 NE2 HIS 557  47.676 39.066 -9.283 1.00 45.62  C3
ATOM 3835 HE2 HIS 557  47.793 39.018 -10.257 1.00  0.00  C3
ATOM 3836 C  HIS 557  45.383 42.249 -5.520 1.00 32.94  C3
ATOM 3837 O  HIS 557  44.256 42.444 -5.934 1.00 33.08  C3
ATOM 3838 N  LEU 558  45.744 42.534 -4.280 1.00 33.05  C3
ATOM 3839 H  LEU 558  46.657 42.356 -3.986 1.00  0.00  C3
ATOM 3840 CA LEU 558  44.817 43.125 -3.348 1.00 31.91  C3
ATOM 3841 CB LEU 558  45.420 43.107 -1.965 1.00 29.25  C3
ATOM 3842 CG LEU 558  44.605 43.615 -0.818 1.00 26.02  C3
ATOM 3843 CD1 LEU 558  43.279 42.883 -0.742 1.00 25.00  C3
ATOM 3844 CD2 LEU 558  45.496 43.571  0.408 1.00 22.86  C3
ATOM 3845 C  LEU 558  44.527 44.521 -3.783 1.00 32.47  C3
ATOM 3846 O  LEU 558  43.402 44.944 -3.596 1.00 33.97  C3
ATOM 3847 N  GLN 559  45.482 45.231 -4.370 1.00 34.36  C3
ATOM 3848 H  GLN 559  46.386 44.855 -4.406 1.00  0.00  C3
ATOM 3849 CA GLN 559  45.255 46.569 -4.912 1.00 36.75  C3
ATOM 3850 CB GLN 559  46.598 47.067 -5.470 1.00 39.63  C3
ATOM 3851 CG GLN 559  46.707 48.543 -5.875 1.00 42.07  C3
ATOM 3852 CD GLN 559  46.530 49.618 -4.793 1.00 41.53  C3
ATOM 3853 OE1 GLN 559  45.961 50.687 -5.057 1.00 41.25  C3
ATOM 3854 NE2 GLN 559  46.951 49.416 -3.561 1.00 37.96  C3
ATOM 3855 HE21 GLN 559  47.271 48.528 -3.311 1.00  0.00  C3
ATOM 3856 HE22 GLN 559  47.001 50.190 -2.967 1.00  0.00  C3
ATOM 3857 C  GLN 559  44.142 46.635 -5.976 1.00 35.22  C3
ATOM 3858 O  GLN 559  43.165 47.404 -5.839 1.00 34.99  C3
ATOM 3859 N  SER 560  44.260 45.817 -7.025 1.00 33.46  C3
ATOM 3860 H  SER 560  45.083 45.292 -7.154 1.00  0.00  C3
ATOM 3861 CA SER 560  43.222 45.683 -8.049 1.00 32.88  C3
ATOM 3862 CB SER 560  43.693 44.776 -9.088 1.00 34.05  C3
ATOM 3863 OG SER 560  45.021 45.174 -9.281 1.00 42.40  C3
ATOM 3864 HG SER 560  45.042 45.996 -9.783 1.00  0.00  C3
ATOM 3865 C  SER 560  41.885 45.133 -7.559 1.00 32.01  C3
ATOM 3866 O  SER 560  40.791 45.582 -7.920 1.00 32.23  C3
ATOM 3867 N  PHE 561  41.969 44.123 -6.710 1.00 29.50  C3
ATOM 3868 H  PHE 561  42.850 43.767 -6.464 1.00  0.00  C3
ATOM 3869 CA PHE 561  40.803 43.529 -6.118 1.00 28.17  C3
ATOM 3870 CB PHE 561  41.237 42.541 -5.040 1.00 26.27  C3
ATOM 3871 CG PHE 561  40.069 41.966 -4.268 1.00 25.68  C3
ATOM 3872 CD1 PHE 561  39.282 40.999 -4.846 1.00 25.44  C3
ATOM 3873 CD2 PHE 561  39.761 42.482 -3.051 1.00 25.45  C3
ATOM 3874 CE1 PHE 561  38.166 40.551 -4.215 1.00 21.49  C3
ATOM 3875 CE2 PHE 561  38.635 42.027 -2.421 1.00 26.89  C3
ATOM 3876 CZ PHE 561  37.853 41.074 -3.008 1.00 24.29  C3
ATOM 3877 C  PHE 561  39.987 44.645 -5.505 1.00 28.81  C3
ATOM 3878 O  PHE 561  38.789 44.697 -5.731 1.00 29.31  C3
ATOM 3879 N  LEU 562  40.672 45.565 -4.797 1.00 28.39  C3
ATOM 3880 H  LEU 562  41.643 45.462 -4.707 1.00  0.00  C3
ATOM 3881 CA LEU 562  40.033 46.617 -4.057 1.00 26.51  C3
ATOM 3882 CB LEU 562  40.964 47.203 -3.074 1.00 23.80  C3
ATOM 3883 CG LEU 562  41.047 46.411 -1.816 1.00 24.85  C3
ATOM 3884 CD1 LEU 562  42.207 46.868 -1.049 1.00 24.07  C3
ATOM 3885 CD2 LEU 562  39.794 46.551 -1.008 1.00 25.13  C3
ATOM 3886 C  LEU 562  39.586 47.669 -4.988 1.00 29.27  C3
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FIG.5CCC

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ATOM  3887 O   LEU  562     38.580  48.304  -4.681  1.00 29.83      C3
ATOM  3888 N   GLU  563     40.239  47.871  -6.115  1.00 30.88      C3
ATOM  3889 H   GLU  563     41.052  47.368  -6.325  1.00  0.00      C3
ATOM  3890 CA  GLU  563     39.738  48.908  -6.966  1.00 36.88      C3
ATOM  3891 CB  GLU  563     40.660  49.142  -8.137  1.00 40.80      C3
ATOM  3892 CG  GLU  563     41.999  49.628  -7.682  1.00 48.55      C3
ATOM  3893 CD  GLU  563     43.148  49.277  -8.619  1.00 55.42      C3
ATOM  3894 OE1 GLU  563     44.301  49.283  -8.135  1.00 57.39      C3
ATOM  3895 OE2 GLU  563     42.886  48.986  -9.808  1.00 56.44      C3
ATOM  3896 C   GLU  563     38.375  48.469  -7.466  1.00 39.02      C3
ATOM  3897 O   GLU  563     37.388  49.170  -7.270  1.00 39.09      C3
ATOM  3898 N   VAL  564     38.289  47.255  -8.030  1.00 42.30      C3
ATOM  3899 H   VAL  564     39.107  46.714  -8.074  1.00  0.00      C3
ATOM  3900 CA  VAL  564     37.052  46.683  -8.558  1.00 41.84      C3
ATOM  3901 CB  VAL  564     37.333  45.255  -9.041  1.00 42.27      C3
ATOM  3902 CG1 VAL  564     36.055  44.538  -9.435  1.00 41.17      C3
ATOM  3903 CG2 VAL  564     38.283  45.348 -10.241  1.00 42.11      C3
ATOM  3904 C   VAL  564     36.030  46.709  -7.442  1.00 41.68      C3
ATOM  3905 O   VAL  564     34.892  47.015  -7.697  1.00 42.34      C3
ATOM  3906 N   SER  565     36.419  46.501  -6.206  1.00 42.75      C3
ATOM  3907 H   SER  565     37.333  46.173  -6.063  1.00  0.00      C3
ATOM  3908 CA  SER  565     35.562  46.602  -5.064  1.00 44.85      C3
ATOM  3909 CB  SER  565     36.344  46.013  -3.894  1.00 46.54      C3
ATOM  3910 OG  SER  565     35.590  45.714  -2.731  1.00 51.75      C3
ATOM  3911 HG  SER  565     35.060  46.481  -2.491  1.00  0.00      C3
ATOM  3912 C   SER  565     35.167  48.063  -4.871  1.00 45.70      C3
ATOM  3913 O   SER  565     34.038  48.287  -4.446  1.00 46.87      C3
ATOM  3914 N   TYR  566     35.965  49.093  -5.146  1.00 47.59      C3
ATOM  3915 H   TYR  566     36.893  48.908  -5.386  1.00  0.00      C3
ATOM  3916 CA  TYR  566     35.518  50.474  -5.086  1.00 49.68      C3
ATOM  3917 CB  TYR  566     36.765  51.362  -5.164  1.00 56.17      C3
ATOM  3918 CG  TYR  566     36.715  52.622  -6.007  1.00 64.64      C3
ATOM  3919 CD1 TYR  566     37.264  52.538  -7.278  1.00 69.53      C3
ATOM  3920 CE1 TYR  566     37.212  53.613  -8.151  1.00 73.71      C3
ATOM  3921 CD2 TYR  566     36.109  53.797  -5.569  1.00 67.98      C3
ATOM  3922 CE2 TYR  566     36.048  54.888  -6.441  1.00 72.92      C3
ATOM  3923 CZ  TYR  566     36.599  54.787  -7.735  1.00 75.29      C3
ATOM  3924 OH  TYR  566     36.538  55.838  -8.652  1.00 77.42      C3
ATOM  3925 HH  TYR  566     36.905  55.565  -9.494  1.00  0.00      C3
ATOM  3926 C   TYR  566     34.524  50.696  -6.217  1.00 48.48      C3
ATOM  3927 O   TYR  566     33.545  51.376  -5.950  1.00 46.35      C3
ATOM  3928 N   ALA  567     34.679  50.115  -7.417  1.00 49.14      C3
ATOM  3929 H   ALA  567     35.512  49.625  -7.572  1.00  0.00      C3
ATOM  3930 CA  ALA  567     33.670  50.165  -8.490  1.00 52.09      C3
ATOM  3931 CB  ALA  567     34.210  49.574  -9.788  1.00 48.37      C3
ATOM  3932 C   ALA  567     32.315  49.449  -8.238  1.00 55.31      C3
ATOM  3933 O   ALA  567     31.226  50.008  -8.501  1.00 56.87      C3
ATOM  3934 N   VAL  568     32.247  48.211  -7.736  1.00 57.66      C3
ATOM  3935 H   VAL  568     33.083  47.729  -7.564  1.00  0.00      C3
ATOM  3936 CA  VAL  568     30.980  47.573  -7.490  1.00 59.61      C3
ATOM  3937 CB  VAL  568     31.119  46.031  -7.339  1.00 58.96      C3
ATOM  3938 CG1 VAL  568     31.239  45.508  -5.911  1.00 60.27      C3
ATOM  3939 CG2 VAL  568     29.851  45.471  -7.922  1.00 60.44      C3
ATOM  3940 C   VAL  568     30.393  48.177  -6.245  1.00 62.66      C3
ATOM  3941 O   VAL  568     29.174  48.154  -6.180  1.00 64.78      C3
ATOM  3942 N   LEU  569     31.075  48.737  -5.248  1.00 66.15      C3
ATOM  3943 H   LEU  569     32.058  48.719  -5.243  1.00  0.00      C3
ATOM  3944 CA  LEU  569     30.359  49.334  -4.123  1.00 69.85      C3
ATOM  3945 CB  LEU  569     31.285  49.858  -3.023  1.00 69.91      C3
ATOM  3946 CG  LEU  569     32.007  48.887  -2.095  1.00 70.17      C3
ATOM  3947 CD1 LEU  569     32.847  49.687  -1.140  1.00 70.19      C3
ATOM  3948 CD2 LEU  569     31.039  48.054  -1.286  1.00 70.56      C3
ATOM  3949 C   LEU  569     29.567  50.509  -4.667  1.00 72.69      C3
ATOM  3950 O   LEU  569     28.365  50.553  -4.425  1.00 73.80      C3
ATOM  3951 N   ARG  570     30.180  51.391  -5.479  1.00 75.95      C3
ATOM  3952 H   ARG  570     31.153  51.299  -5.580  1.00  0.00      C3
ATOM  3953 CA  ARG  570     29.510  52.498  -6.173  1.00 78.78      C3
ATOM  3954 CB  ARG  570     30.399  53.068  -7.308  1.00 80.07      C3
ATOM  3955 CG  ARG  570     29.658  54.222  -7.997  1.00 84.16      C3
ATOM  3956 CD  ARG  570     29.976  54.744  -9.417  1.00 85.66      C3
ATOM  3957 NE  ARG  570     28.892  55.690  -9.737  1.00 85.67      C3
ATOM  3958 HE  ARG  570     27.971  55.354  -9.727  1.00  0.00      C3
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FIG.5DDD

ATOM 3959 CZ ARG 570 29.051 56.991 -10.026 1.00 85.06 C3
ATOM 3960 NH1 ARG 570 30.240 57.590 -10.082 1.00 84.43 C3
ATOM 3961 HH11 ARG 570 31.069 57.056 -9.908 1.00 0.00 C3
ATOM 3962 HH12 ARG 570 30.295 58.561 -10.314 1.00 0.00 C3
ATOM 3963 NH2 ARG 570 27.958 57.736 -10.154 1.00 84.57 C3
ATOM 3964 HH21 ARG 570 27.059 57.316 -10.030 1.00 0.00 C3
ATOM 3965 HH22 ARG 570 28.042 58.708 -10.375 1.00 0.00 C3
ATOM 3966 C ARG 570 28.201 52.009 -6.812 1.00 79.92 C3
ATOM 3967 O ARG 570 27.107 52.565 -6.709 1.00 79.61 C3
ATOM 3968 N HIS 571 28.362 50.900 -7.511 1.00 81.35 C3
ATOM 3969 H HIS 571 29.214 50.417 -7.440 1.00 0.00 C3
ATOM 3970 CA HIS 571 27.247 50.306 -8.197 1.00 82.75 C3
ATOM 3971 CB HIS 571 27.882 49.274 -9.167 1.00 83.42 C3
ATOM 3972 CG HIS 571 28.633 50.029 -10.280 1.00 85.08 C3
ATOM 3973 CD2 HIS 571 28.921 49.529 -11.532 1.00 85.81 C3
ATOM 3974 ND1 HIS 571 29.074 51.303 -10.268 1.00 86.25 C3
ATOM 3975 HD1 HIS 571 29.080 51.900 -9.489 1.00 0.00 C3
ATOM 3976 CE1 HIS 571 29.595 51.595 -11.439 1.00 86.01 C3
ATOM 3977 NE2 HIS 571 29.494 50.518 -12.187 1.00 86.28 C3
ATOM 3978 HE2 HIS 571 29.801 50.468 -13.119 1.00 0.00 C3
ATOM 3979 C HIS 571 26.225 49.759 -7.195 1.00 83.31 C3
ATOM 3980 O HIS 571 25.075 50.194 -7.301 1.00 84.06 C3
ATOM 3981 N LEU 572 26.540 48.963 -6.158 1.00 83.11 C3
ATOM 3982 H LEU 572 27.474 48.824 -5.915 1.00 0.00 C3
ATOM 3983 CA LEU 572 25.527 48.457 -5.241 1.00 83.71 C3
ATOM 3984 CB LEU 572 26.085 47.267 -4.454 1.00 83.57 C3
ATOM 3985 CG LEU 572 25.439 45.884 -4.721 1.00 83.79 C3
ATOM 3986 CD1 LEU 572 25.783 45.386 -6.127 1.00 84.16 C3
ATOM 3987 CD2 LEU 572 25.958 44.866 -3.714 1.00 84.08 C3
ATOM 3988 C LEU 572 24.997 49.511 -4.261 1.00 84.78 C3
ATOM 3989 O LEU 572 24.265 49.192 -3.295 1.00 84.85 C3
ATOM 3990 N ALA 573 25.349 50.796 -4.483 1.00 85.56 C3
ATOM 3991 H ALA 573 26.020 50.980 -5.174 1.00 0.00 C3
ATOM 3992 CA ALA 573 24.822 51.925 -3.721 1.00 85.90 C3
ATOM 3993 CB ALA 573 25.600 53.207 -3.970 1.00 85.79 C3
ATOM 3994 C ALA 573 23.373 52.245 -4.057 1.00 87.21 C3
ATOM 3995 OT1 ALA 573 22.610 52.413 -3.099 1.00 88.33 C3
ATOM 3996 OT2 ALA 573 23.022 52.309 -5.248 1.00 88.34 C3
ATOM 3997 OH2 H2O 603 26.735 24.280 5.161 1.00 27.42 W
ATOM 3998 H1 H2O 603 27.332 24.335 4.407 1.00 0.00 W
ATOM 3999 H2 H2O 603 26.288 23.435 4.992 1.00 0.00 W
ATOM 4000 OH2 H2O 605 47.880 37.960 12.073 1.00 56.30 W
ATOM 4001 H1 H2O 605 47.789 37.874 13.031 1.00 0.00 W
ATOM 4002 H2 H2O 605 46.980 37.858 11.753 1.00 0.00 W
ATOM 4003 OH2 H2O 607 40.001 49.224 7.214 1.00 40.04 W
ATOM 4004 H1 H2O 607 40.471 48.761 7.909 1.00 0.00 W
ATOM 4005 H2 H2O 607 40.123 48.642 6.457 1.00 0.00 W
ATOM 4006 OH2 H2O 610 59.883 42.530 -9.698 1.00 38.90 W
ATOM 4007 H1 H2O 610 60.512 41.833 -9.477 1.00 0.00 W
ATOM 4008 H2 H2O 610 59.189 42.046 -10.160 1.00 0.00 W
ATOM 4009 OH2 H2O 611 57.178 35.940 -14.220 1.00 34.63 W
ATOM 4010 H1 H2O 611 57.174 36.545 -14.974 1.00 0.00 W
ATOM 4011 H2 H2O 611 57.989 36.211 -13.757 1.00 0.00 W
ATOM 4012 OH2 H2O 612 25.793 27.337 19.130 1.00 29.21 W
ATOM 4013 H1 H2O 612 26.709 27.661 19.145 1.00 0.00 W
ATOM 4014 H2 H2O 612 25.762 26.792 19.929 1.00 0.00 W
ATOM 4015 OH2 H2O 615 29.766 34.284 9.444 1.00 45.03 W
ATOM 4016 H1 H2O 615 30.017 34.618 10.308 1.00 0.00 W
ATOM 4017 H2 H2O 615 29.113 33.592 9.660 1.00 0.00 W
ATOM 4018 OH2 H2O 617 37.316 40.012 10.872 1.00 35.21 W
ATOM 4019 H1 H2O 617 36.600 40.017 11.519 1.00 0.00 W
ATOM 4020 H2 H2O 617 37.944 39.376 11.259 1.00 0.00 W
ATOM 4021 OH2 H2O 619 40.370 52.041 -7.387 1.00 29.62 W
ATOM 4022 H1 H2O 619 40.672 52.724 -6.779 1.00 0.00 W
ATOM 4023 H2 H2O 619 39.505 51.810 -7.052 1.00 0.00 W
ATOM 4024 OH2 H2O 621 27.903 32.440 10.664 1.00 39.99 W
ATOM 4025 H1 H2O 621 27.553 33.207 11.141 1.00 0.00 W
ATOM 4026 H2 H2O 621 27.929 31.808 11.398 1.00 0.00 W
ATOM 4027 OH2 H2O 622 25.057 31.972 13.675 1.00 32.70 W
ATOM 4028 H1 H2O 622 24.393 32.417 14.215 1.00 0.00 W
ATOM 4029 H2 H2O 622 24.469 31.428 13.112 1.00 0.00 W
ATOM 4030 OH2 H2O 623 20.791 28.583 14.218 1.00 50.17 W

FIG.5EEE

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ATOM  4031 H1  H2O  623    20.499 28.803 13.325 1.00 0.00      W
ATOM  4032 H2  H2O  623    19.939 28.549 14.688 1.00 0.00      W
ATOM  4033 OH2 H2O  625    22.680 78.881  2.761 1.00 40.48    W
ATOM  4034 H1  H2O  625    21.938 78.856  3.375 1.00 0.00      W
ATOM  4035 H2  H2O  625    22.266 79.246  1.970 1.00 0.00      W
ATOM  4036 OH2 H2O  626    39.689 36.486  9.730 1.00 23.36    W
ATOM  4037 H1  H2O  626    39.090 35.724  9.672 1.00 0.00      W
ATOM  4038 H2  H2O  626    39.627 36.872  8.853 1.00 0.00      W
ATOM  4039 OH2 H2O  627    42.035 78.320  5.697 1.00 46.19    W
ATOM  4040 H1  H2O  627    42.416 77.450  5.832 1.00 0.00      W
ATOM  4041 H2  H2O  627    41.243 78.146  5.181 1.00 0.00      W
ATOM  4042 OH2 H2O  631    47.227 31.440  6.299 1.00 34.17    W
ATOM  4043 H1  H2O  631    47.533 32.209  5.809 1.00 0.00      W
ATOM  4044 H2  H2O  631    47.442 30.713  5.714 1.00 0.00      W
ATOM  4045 OH2 H2O  636    24.043 65.423 -0.336 1.00 73.38    W
ATOM  4046 H1  H2O  636    24.179 65.781 -1.228 1.00 0.00      W
ATOM  4047 H2  H2O  636    23.469 66.096  0.054 1.00 0.00      W
ATOM  4048 OH2 H2O  638    38.984 67.955 -11.226 1.00 29.97    W
ATOM  4049 H1  H2O  638    38.283 67.402 -11.580 1.00 0.00      W
ATOM  4050 H2  H2O  638    39.568 68.046 -11.998 1.00 0.00      W
ATOM  4051 OH2 H2O  639    27.930 66.675 -7.733 1.00 43.40     W
ATOM  4052 H1  H2O  639    28.192 67.028 -6.876 1.00 0.00      W
ATOM  4053 H2  H2O  639    26.975 66.791 -7.705 1.00 0.00      W
ATOM  4054 OH2 H2O  643    50.619 62.802  0.813 1.00 36.55    W
ATOM  4055 H1  H2O  643    51.575 62.904  0.824 1.00 0.00      W
ATOM  4056 H2  H2O  643    50.301 63.665  0.525 1.00 0.00      W
ATOM  4057 OH2 H2O  646    62.897 38.367  3.759 1.00 73.55    W
ATOM  4058 H1  H2O  646    62.414 38.098  2.978 1.00 0.00      W
ATOM  4059 H2  H2O  646    62.244 38.247  4.461 1.00 0.00      W
ATOM  4060 OH2 H2O  650    29.587 68.480 -9.555 1.00 65.67    W
ATOM  4061 H1  H2O  650    28.846 68.630 -10.148 1.00 0.00     W
ATOM  4062 H2  H2O  650    29.180 67.844 -8.936 1.00 0.00      W
ATOM  4063 OH2 H2O  652    51.408 56.331  4.056 1.00 62.90    W
ATOM  4064 H1  H2O  652    50.718 56.353  3.365 1.00 0.00      W
ATOM  4065 H2  H2O  652    51.052 55.671  4.648 1.00 0.00      W
ATOM  4066 OH2 H2O  653    49.404 56.022  2.161 1.00 51.28    W
ATOM  4067 H1  H2O  653    49.442 55.351  1.474 1.00 0.00      W
ATOM  4068 H2  H2O  653    49.323 56.829  1.630 1.00 0.00      W
ATOM  4069 OH2 H2O  654    68.215 42.294 -2.563 1.00 40.77    W
ATOM  4070 H1  H2O  654    68.347 41.745 -1.777 1.00 0.00      W
ATOM  4071 H2  H2O  654    68.189 43.181 -2.190 1.00 0.00      W
ATOM  4072 OH2 H2O  655    66.374 40.425 -2.489 1.00 42.31    W
ATOM  4073 H1  H2O  655    66.936 41.162 -2.766 1.00 0.00      W
ATOM  4074 H2  H2O  655    66.452 39.841 -3.252 1.00 0.00      W
ATOM  4075 OH2 H2O  656    66.927 41.428 -5.011 1.00 44.08    W
ATOM  4076 H1  H2O  656    66.207 42.071 -4.989 1.00 0.00      W
ATOM  4077 H2  H2O  656    67.542 41.824 -4.374 1.00 0.00      W
ATOM  4078 OH2 H2O  657    40.371 57.111  5.730 1.00 66.56    W
ATOM  4079 H1  H2O  657    39.958 56.259  5.613 1.00 0.00      W
ATOM  4080 H2  H2O  657    40.021 57.651  5.014 1.00 0.00      W
ATOM  4081 OH2 H2O  658    48.780 47.580 -3.122 1.00 52.09    W
ATOM  4082 H1  H2O  658    48.811 46.671 -3.438 1.00 0.00      W
ATOM  4083 H2  H2O  658    49.568 47.955 -3.542 1.00 0.00      W
ATOM  4084 OH2 H2O  663    29.095 62.889  1.825 1.00 39.23    W
ATOM  4085 H1  H2O  663    29.380 62.827  2.739 1.00 0.00      W
ATOM  4086 H2  H2O  663    28.377 63.526  1.887 1.00 0.00      W
ATOM  4087 OH2 H2O  664    27.132 25.640  7.430 1.00 50.65    W
ATOM  4088 H1  H2O  664    26.870 24.838  7.876 1.00 0.00      W
ATOM  4089 H2  H2O  664    27.001 25.362  6.496 1.00 0.00      W
ATOM  4090 OH2 H2O  665    23.367 30.554 12.167 1.00 49.69    W
ATOM  4091 H1  H2O  665    24.026 30.006 11.707 1.00 0.00      W
ATOM  4092 H2  H2O  665    22.941 31.016 11.438 1.00 0.00      W
ATOM  4093 OH2 H2O  666    46.015 32.192 10.179 1.00 66.86    W
ATOM  4094 H1  H2O  666    46.060 31.519  9.497 1.00 0.00      W
ATOM  4095 H2  H2O  666    45.411 31.827 10.833 1.00 0.00      W
ATOM  4096 OH2 H2O  667    38.943 37.883 11.978 1.00 47.87    W
ATOM  4097 H1  H2O  667    39.367 37.487 11.188 1.00 0.00      W
ATOM  4098 H2  H2O  667    38.521 37.114 12.362 1.00 0.00      W
ATOM  4099 OH2 H2O  671    33.437 58.101  2.269 1.00 46.65    W
ATOM  4100 H1  H2O  671    33.555 57.162  2.433 1.00 0.00      W
ATOM  4101 H2  H2O  671    33.962 58.514  2.961 1.00 0.00      W
ATOM  4102 OH2 H2O  672    27.551 31.314 20.022 1.00 30.15    W
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FIG.5FFF

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ATOM  4103 H1  H2O  672      27.929  32.042  20.533  1.00  0.00      W
ATOM  4104 H2  H2O  672      26.845  31.764  19.552  1.00  0.00      W
ATOM  4105 OH2 H2O  673      25.714  36.908  21.385  1.00 36.95      W
ATOM  4106 H1  H2O  673      24.806  37.123  21.637  1.00  0.00      W
ATOM  4107 H2  H2O  673      25.599  36.284  20.654  1.00  0.00      W
ATOM  4108 OH2 H2O  674      38.244  66.897  12.076  1.00 57.36      W
ATOM  4109 H1  H2O  674      37.773  67.536  12.626  1.00  0.00      W
ATOM  4110 H2  H2O  674      38.153  66.104  12.618  1.00  0.00      W
ATOM  4111 OH2 H2O  675      35.762  36.553  -3.986  1.00 58.40      W
ATOM  4112 H1  H2O  675      35.600  37.449  -3.677  1.00  0.00      W
ATOM  4113 H2  H2O  675      35.549  36.642  -4.923  1.00  0.00      W
ATOM  4114 OH2 H2O  676      30.689  32.814  25.675  1.00 59.30      W
ATOM  4115 H1  H2O  676      30.093  33.571  25.680  1.00  0.00      W
ATOM  4116 H2  H2O  676      31.550  33.214  25.540  1.00  0.00      W
END
```

FIG. 6A

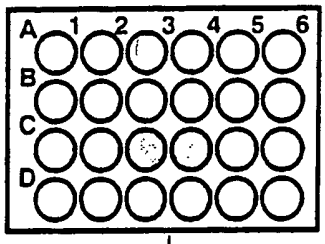


FIG. 6B

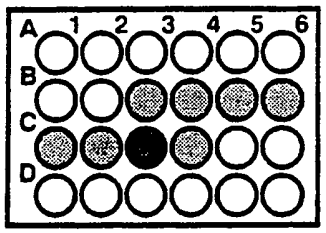
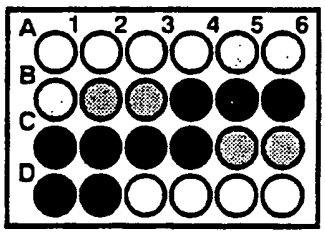


FIG. 6C



INTERNATIONAL SEARCH REPORT

Inter nal Application No
PCT/US 94/00913

A. CLASSIFICATION OF SUBJECT MATTER
IPC 5 C12N15/27 C07K3/00 C12P21/02 C07K13/00 G06F15/60

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 5 C12N C07K C12P

Documentation searched other than mimmum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

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Date of the actual completion of the international search	Date of mailing of the international search report
11 May 1994	01 -06- 1994

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Le Cornec, N

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